JOURNAL

of the

INDIAN MEDICAL ASSOCIATION

VOLUME 35 NUMBER 1 CALCUTTA JULY 1, 1960

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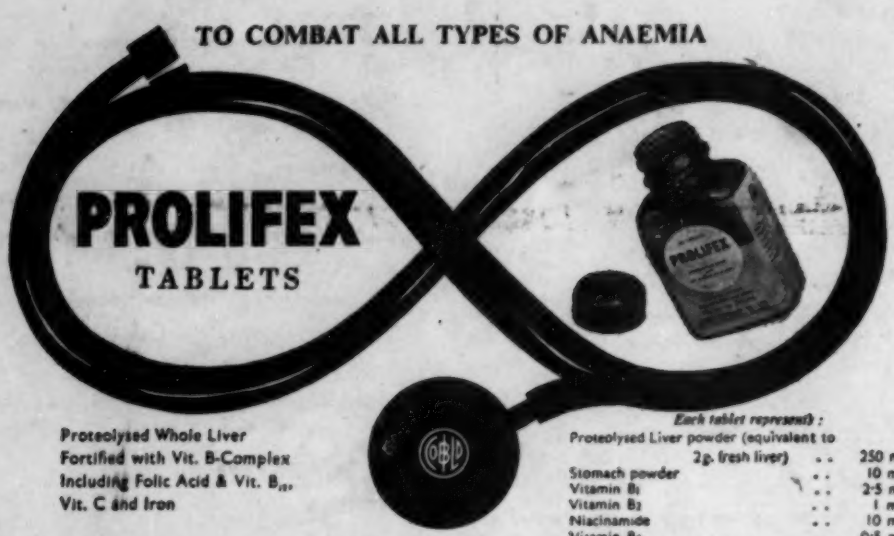

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TABLE OF CONTENTS

ORIGINAL ARTICLES:	Page
1. Acute Epidemic Encephalitis in Children (Lucknow, 1958): A Clinical Study—P. C. Bajpai, S. K. Dikshit, J. C. Sharma, N. P. Gupta and K. K. Govil	1
2. Haemoglobin E Disease in Bengalees—Sushiela Swarup, S. K. Ghosh and J. B. Chatterjea ...	13
3. Rarer Causes of Cor Pulmonale (Report of Two Cases)—Souren Chakraverty and B. C. Katiyar	16
4. A Study on Coronary Vascular System —S. K. Chatterjee and M. K. Roy ...	18
PRACTITIONERS' SERIES:	
Cirrhosis of the Liver—Robert Hellig ...	20
SPECIAL ARTICLE:	
The Role of Anthropology in Social and Preventive Medicine—Khwaja Arif Hasan and B. G. Prasad	23

CASE NOTES:	Page
1. Neurological Manifestations of Sarcoidosis —N. N. Gupta and B. C. Katiyar ...	27
2. Carotid Body Tumour—C. M. Rangam and J. C. Gupta	31
EDITORIAL:	
The Problem of Medical Education in Our Country	32
I. M. A. PRESIDENT'S TOUR OF MAHARASHTRA ...	33
GENERAL PRACTICE DIGEST:	
Treatment of Pulmonary Emphysema ...	34
CURRENT MEDICAL LITERATURE ...	35
CURRENT TOPIC:	
The Present Status of Therapy of Plague —S. C. Seal	38
NOTES AND NEWS	45
REVIEWS	46
OBITUARIES	47

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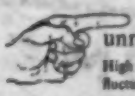

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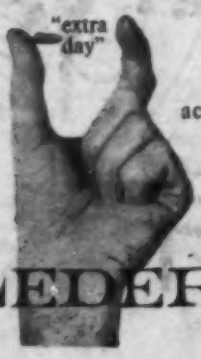

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Index to Advertisers

	Page
Allen & Hanburys Ltd.	xl
Allied Photographics Private Ltd.	xvi
Antiseptic	xxxviii
Alembic Chemical Works Co. Ltd.	xxxix
Bengal Chemical & Pharm. Works Ltd.	Front Cover
Bengal Immunity Co. Ltd.	2nd Cover
Boehringer - Knoll Private Ltd.	ix
Chemo - Pharma Laboratories Ltd.	xii
Corn Products Co. (India) Pvt. Ltd.	xx
Crookes Laboratories Ltd.	xxxiv
Dey's Medical Stores Private Ltd.	ii
East India Pharmaceutical Works Ltd.	xxiv
Eastern Drug Co. Ltd.	xxxii
Franco-Indian Pharma. Pvt. Ltd.	vii, xiii, xvii
G. D. Pharmaceuticals Private Ltd.	xviii
G. D. A. Chemicals Ltd.	xxxviii
Hoechst Pharmaceuticals Pvt. Ltd.	xxvii
Hind Chemicals Limited.	xxxvii
Indian Health Institute & Labo. Ltd.	xxxvii
Imperial Chemical Indus. (I) Pvt. Ltd.	vi, xxvi
Ilford - Selo (India) Pvt. Ltd.	x
International Chemical & Biological Institute Private Ltd.	xxxi
J & J. DeChane	xx
John Wyeth & Brother Ltd.	xi
Kodak Limited.	iv
Khatau Valabhdas & Co.	xv
Khandelwal Laboratories Pvt. Ltd.	xxi
Knox Company (Muller & Phipps (India) Pvt. Ltd.)	xxiii
Lederle Laboratories (I) Pvt. Ltd.	i
Neo-Pharma Private Ltd.	v
Nestle's Products (India) Ltd.	viii
Navaratna Pharma. Laboratories	xxxvii
Oriental Pharmaceutical Indus. Ltd.	iii
Phoenix Drug House Pvt. Ltd. (Fairfield Syndicate (Agency) Pvt. Ltd.)	xii
Pfizer Eastern Corporation (Dumex Private Ltd.)	xxv, xxx
Raptakos, Brett & Co. Pvt. Ltd.	xxxi
Rallis India Limited	xxxv
Ranbaxy & Co. Ltd.	xxxvi
Stadmed Private Ltd.	xviii
Smith Stanistreet & Co. Ltd.	xix
Sarabhai Chemicals	xxii
Suhrid Geigy Trading Private Ltd.	xxix
Smith, Kline & French (India) Ltd.	xxxiii
Trade Wings Private Ltd.	3rd Cover
Therapeutic Pharmaceuticals	xiv
Unichem Laboratories	Back Cover
Voltas Limited	xxviii
Veb Carl Zeiss Jena	xxxiv
Zandu Pharmaceutical Works Ltd.	xxxvi

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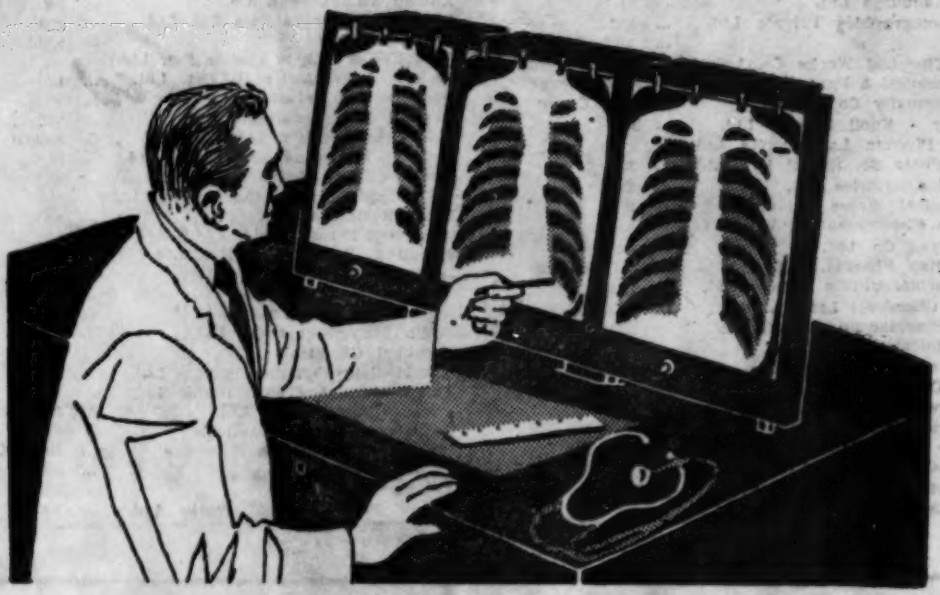

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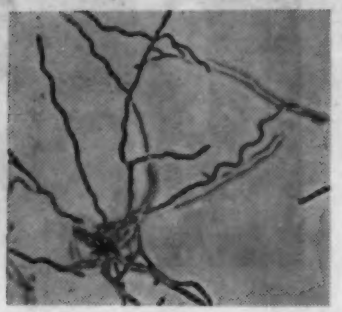

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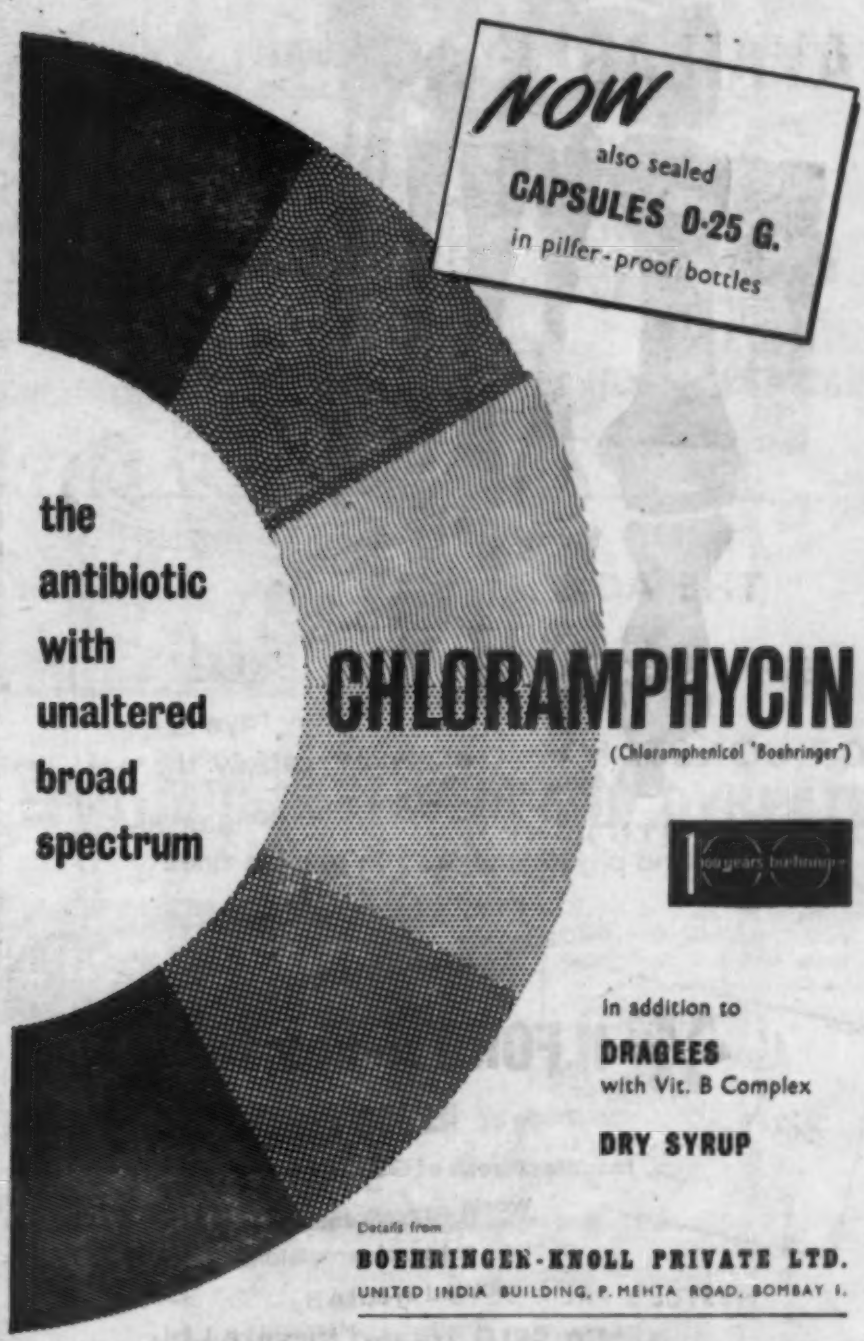

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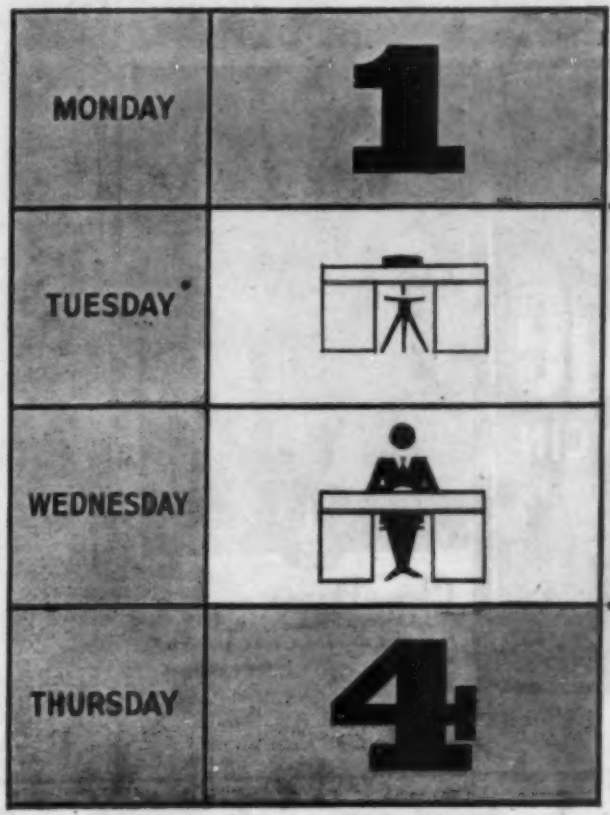

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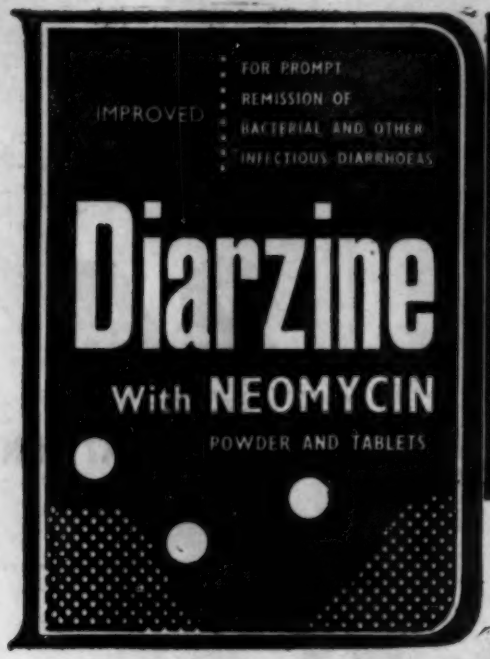

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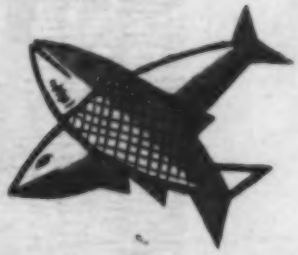

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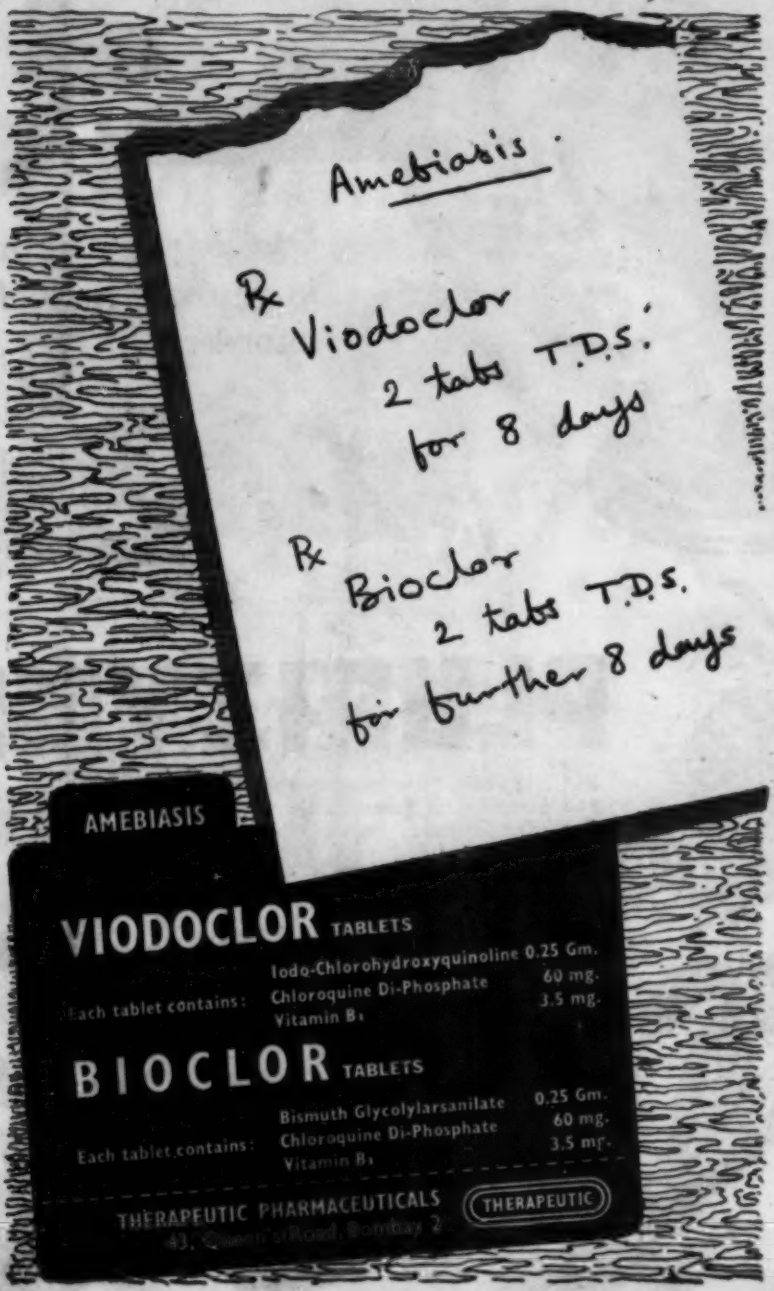
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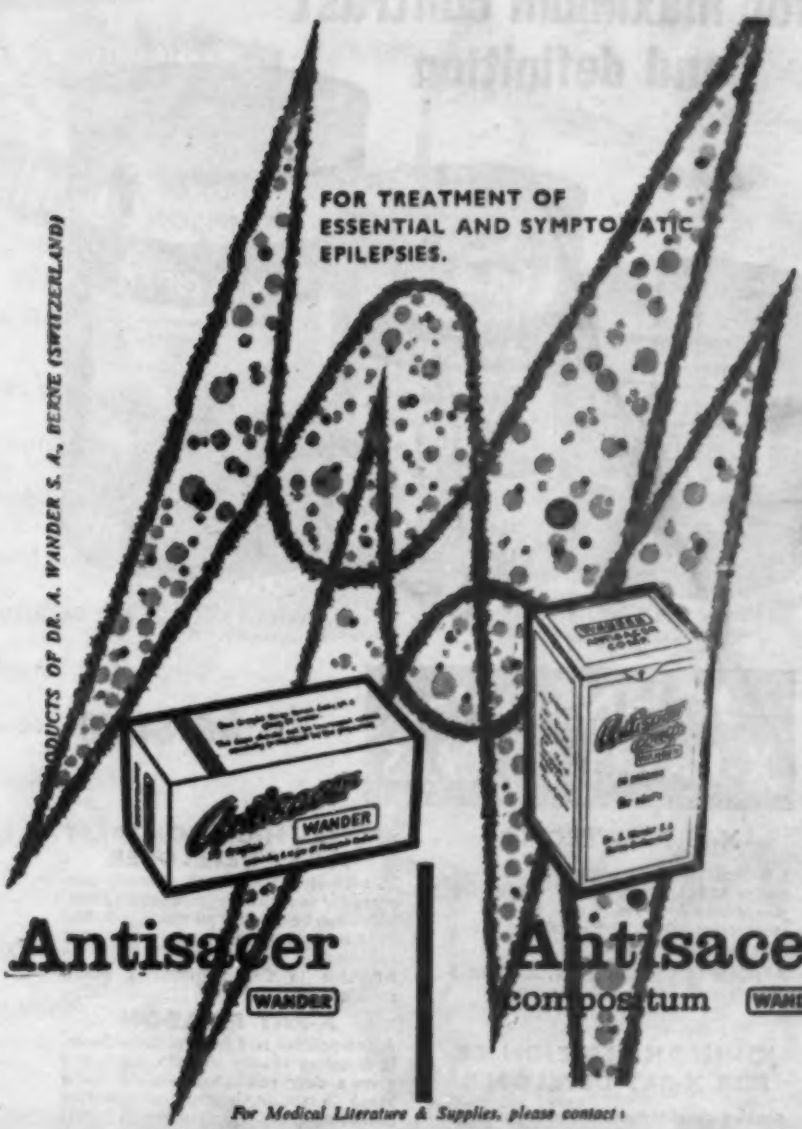

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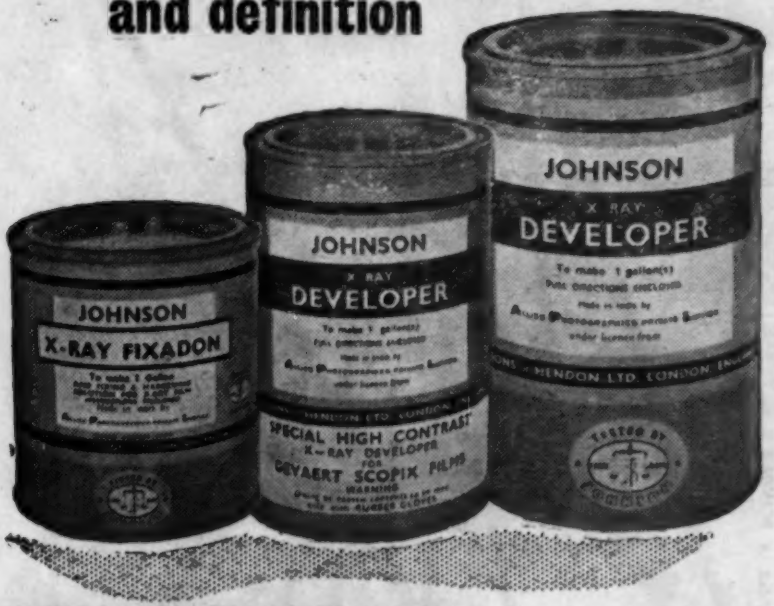

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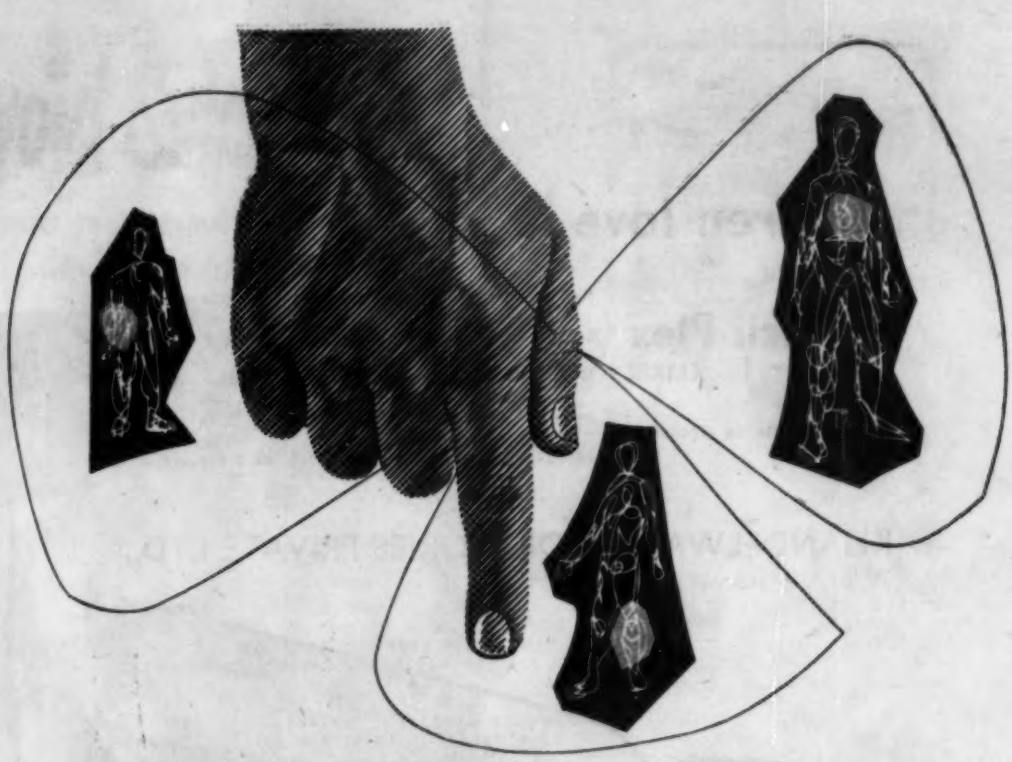

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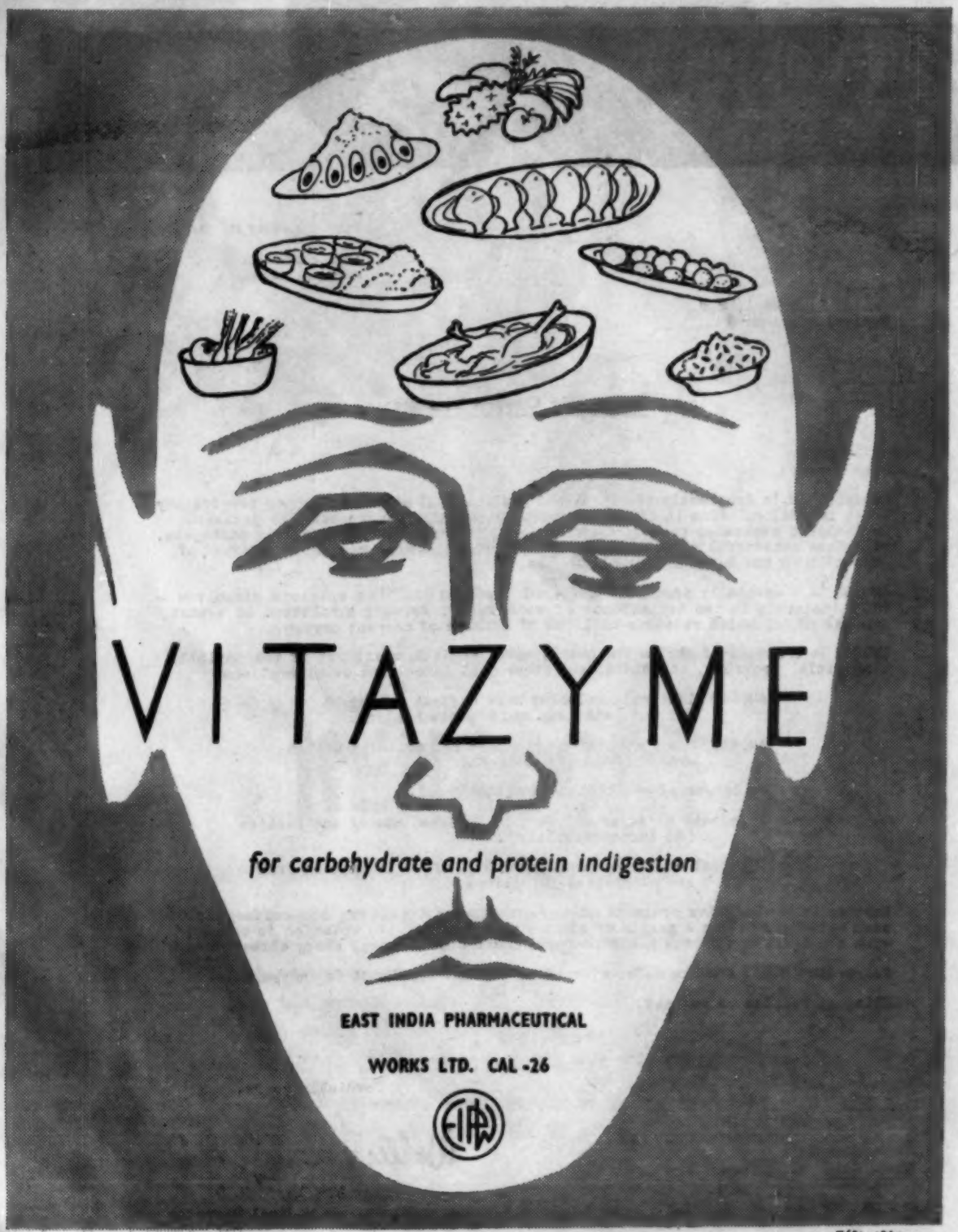
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Journal of the Indian Medical Association

VOLUME 35
NUMBER 1

PUBLISHED TWICE A MONTH
EDITOR—P. K. GUHA, M.B., M.R.C.S. (ENG.), D.O.M.S. (LOND.)

CALCUTTA
JULY 1, 1960

ORIGINAL ARTICLES

ACUTE EPIDEMIC ENCEPHALITIS IN CHILDREN (LUCKNOW, 1958) A CLINICAL STUDY

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INTRODUCTION

An epidemic of encephalitis broke out in children at Lucknow in the first week of July, 1958. Coming in the wake of a similar epidemic which had raged in 1954, a systematic study was planned from the very beginning. Hospital management, public health authorities and the I.C.M.R. were immediately alerted by the Children's Section and an adequate organisation was set up in the shortest possible time. This consisted of three teams, viz., (i) a Clinical Unit from the Children's Hospital for diagnosis and management of the hospitalised cases in the acute phase and the immediate and remote follow-up of all the cases as far as possible, (ii) a Virological Unit handling samples sent by the clinical unit for purposes of isolating and detecting a possible virus and (iii) an Epidemiological and Entomological unit, looking after the distribution of cases, the relevant public health measures, and collection of possible insect vectors. The public and the medical profession were informed of the existing situation through a press statement. An emergency grant for a clinical research fellow and another for the virology team was made available through the courtesy of the I.C.M.R.

Some 301 children were admitted to the Children's Hospital, K. G. Medical College, Lucknow, in 3 months, although sporadic cases were observed afterwards. Eighteen other cases were initially suspected to be suffering from encephalitis but subsequently diagnosed as suffering from conditions like tubercular meningitis, septic meningitis, haemorrhagic smallpox, etc., and were not included in this series. The rate of admission was very high, viz., 66, 58, 50, and 45 cases in the respective four weeks of July, 1958. In the first week of August it showed a fairly steep fall to 25 cases, after which the number of cases went on decreasing until at the end of September (Fig. 1) when the tail end of the epidemic imperceptibly merged with the sporadic cases. It is evident from Fig. 2 that the hospitalised cases of encephalitis made the bulk of total admissions during the first 4 weeks of the epidemic. The need for admission of non-encephalitis cases necessitated expansion of

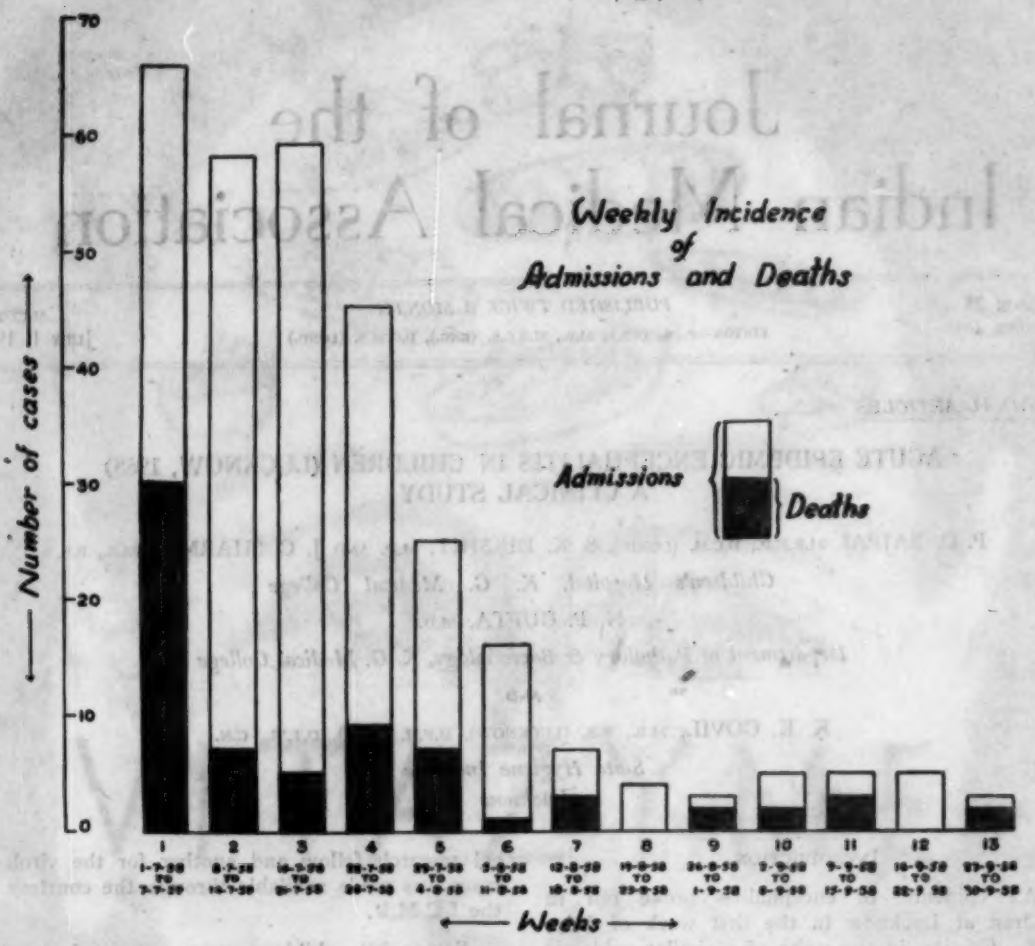

FIG. 1

the hospital beds to three times the existing strength during the epidemic. All the cases attending the children's out-patients department and the casualty room were admitted for a systematic study. The present study only deals with the analysis of cases from the acute phase of the epidemic, as made by the Clinical Unit.

EPIDEMIOLOGY

The epidemiological aspects have been dealt with in detail in a separate paper (Govil *et al*, 1959). However, a brief note on it is given below. Cases were admitted from all the municipal wards of Lucknow, as also from relatively distantly situated places in the city. Within a week the case incidence increased in all the municipal areas. There was no definite relationship between the case incidence of a locality and the density of its population. It is interesting to recall that this as well as other reported epidemics has almost invariably occurred during the summer.

In general the environmental sanitation of the homes visited was not up to the mark, and often the ventilation was found to be inadequate. Being aware of the importance of arthropods in the epidemic outbreaks of encephalitis, a limited entomological survey was undertaken from the affected houses. This yielded an assortment of insects, the commonest being *Musca vicina* (the common housefly), others being the different types of mosquito (Anopheles, Culex, *Aedes aegypti*). After the catch these insects were subjected to a virological examination, and were found to be negative. Also no definite association of the present epidemic with viral infections in cattle could be established.

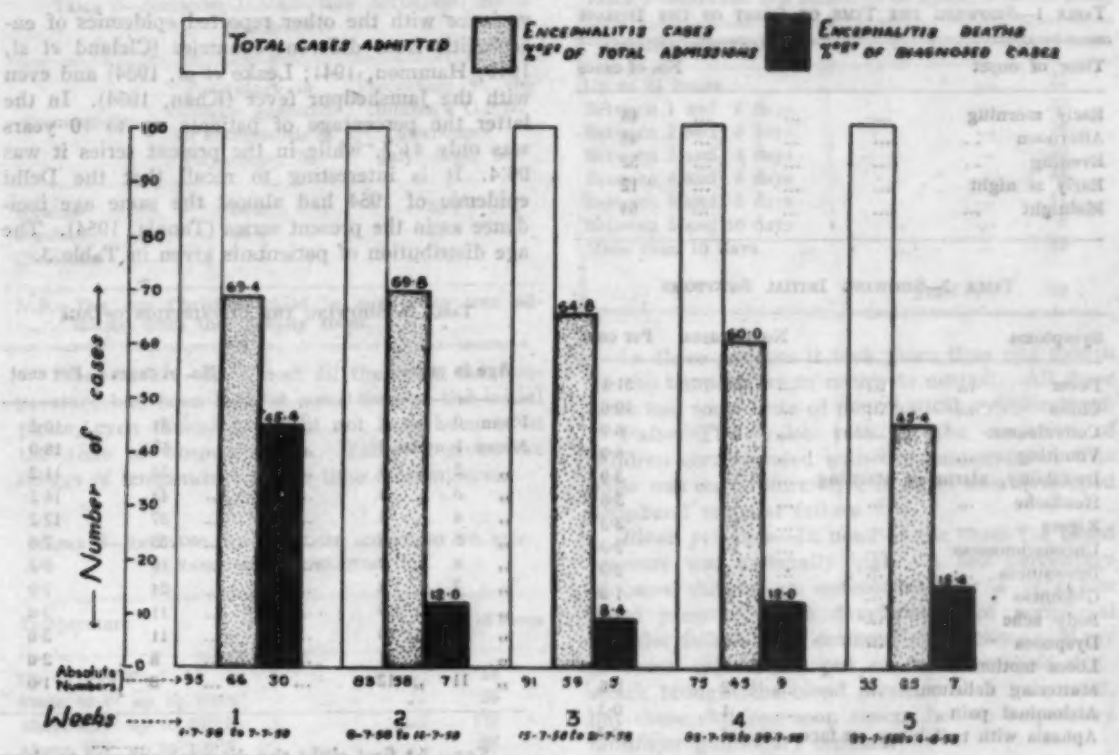

FIG. 2

A follow-up done by the clinical team in the affected families showed the frequency of suspected multiple cases to be about 18·6 per cent, the usual duration between the onset of symptoms in the two cases being zero to 15 days (two cases being spotted on the same day at an interval of a few hours). The diagnosis of encephalitis in some of these cases was made in retrospect on the clinical features described by the parents. In at least two families one child had already died of encephalitis while the other was brought for admission to the hospital.

CLINICAL FEATURES

Four comatose patients admitted with similar onset within 24 hours on 1st July, 1958, made us suspect that an epidemic might be in the offing. A wealth of clinical material was collected within a few weeks of the onset of the epidemic, and with the help of a carefully planned proforma made at the very beginning could we systematically study and follow up the clinical aspects of the epidemic.

Onset—In the majority of cases (89·4 per cent) the onset was fairly uniform and abrupt. The best nourished child of the family and often their only child was attacked. A history of significant past illness was rarely available, and there was little evidence or account of any symptoms immediately preceding the clinical onset, viz., upper respiratory tract infection, gastro-intestinal upset, rash, etc., which could be labelled as prodromata of this disease. In 32 cases (10·6 per cent) the onset was not so abrupt and stormy as in others, and the complete symptom complex was built up rather quickly taking one to two days. In relatively older children the time of onset, as told by the parents, was mostly in the afternoon or evening, after an active day at home or school. In the younger age group it began mostly in the night or during the early hours of the morning. Table 1 shows roughly the time of onset in the cases in which a reliable answer was forthcoming.

Initial manifestations—The more important initial symptoms are given in Table 2.

As described by the attendants, any one of the above symptoms appeared first, with all its suddenness, followed in quick succession by others, culminating into a complete clinical syndrome of encephalitis. Besides these, some very interesting modes of onset were seen ; for example twitchings

TABLE 1—SHOWING THE TIME OF ONSET OF THE DISEASE

Time of onset	No. of cases
Early morning	48
Afternoon	45
Evening	52
Early at night	12
Midnight	84

TABLE 2—SHOWING INITIAL SYMPTOMS

Symptoms	No. of cases	Per cent
Fever	154	51·1
Chills	32	10·6
Convulsions	21	6·9
Vomiting	18	5·9
Irritability, alarm or startling ...	12	3·9
Headache	11	3·6
Rigors	10	3·3
Unconsciousness	10	3·3
Drowsiness	9	2·9
Giddiness	6	1·9
Body ache	5	1·6
Dyspnoea	5	1·6
Loose motions	4	1·3
Muttering delirium	2	0·6
Abdominal pain	1	0·3
Aphasia with twitchings on face ...	1	0·3
Total ...	301	

on one side of face in one child, left-sided hemiparesis in another and weakness of one of the limbs in yet another case. Assumption of an attitude of flexion with tremors was observed in two children who later showed a complete picture of extrapyramidal syndrome. Abruptness of onset was dramatic in a girl of about 6 years who gave a sudden loud cry and immediately fell down unconscious. Other signs and symptoms gradually made their appearance. History of exertion or exposure was frequently forthcoming. One child, soon after a bath in the river, developed high fever followed by unconsciousness and convulsions.

Among uncommon symptoms complained of by some individuals during the course of the illness were pain in right axilla, pain in right superior extremity, pain in both right limbs, etc. There was epistaxis in one case and blood-stained vomit in another. Urticarial rash was observed in one case.

Age—In this epidemic, only children were picked up, and not a single adult with this disease was admitted in the G.M. and associated group of Hospitals, Lucknow. This observation is in variance with the other reported epidemics of encephalitis from different countries (Cleland *et al*, 1919; Hammon, 1941; Leake *et al*, 1934) and even with the Jamshedpur fever (Khan, 1954). In the latter the percentage of patients up to 10 years was only 41·7, while in the present series it was 96·4. It is interesting to recall that the Delhi epidemic of 1954 had almost the same age incidence as in the present series (Taneja, 1954). The age distribution of patients is given in Table 3.

TABLE 3—SHOWING THE DISTRIBUTION OF AGE

Age in years	No. of cases	Per cent
From 0 to 1	31	10·2
Above 1 up to 2	57	18·9
„ 2 „ 3	34	11·2
„ 3 „ 4	43	14·2
„ 4 „ 5	37	12·2
„ 5 „ 6	23	7·6
„ 6 „ 7	19	6·3
„ 7 „ 8	24	7·9
„ 8 „ 9	11	3·6
„ 9 „ 10	11	3·6
„ 10 „ 11	8	2·6
„ 11 „ 12	3	1·0

Sex—At first sight the diseaese appears to show a male sex preponderance (61·3 per cent male and 39·7 per cent female). However, it can be easily understood by a study of Table 4 which gives a comparative sex ratio of encephalitis cases and those attending the Children's O.P.D. during the same period. Although other authors from India and abroad (Cleland *et al*, 1919 ; Swami and Chari, 1955 ; Gour, 1954) have reported a sex predilection, no comparative analysis of similar nature is available. The sexes were found to be equally affected in the epidemic of encphalitis in St. Louis (Leake *et al*, 1934).

TABLE 4—SHOWING THE DISTRIBUTION OF SEX

Sex	July '58		August '58		September '58	
	Male %	Female %	Male %	Female %	Male %	Female %
Encephalitis cases	61·8	38·2	59·5	40·5	55·5	44·5
O.P.D. cases	63·7	36·3	60·3	39·7	62·7	37·3

Community—Table 5 shows communitywise incidence of the illness.

TABLE 5—SHOWING DISTRIBUTION ACCORDING TO COMMUNITY

Communities	Percentage in children admitted for encephalitis in July—Sept. '58	Percentage in the children's O.P.D. attendance July—Sept. '58
Hindus ...	63·2	50·7
Muslims ...	36·5	49·3
Christians ...	0·3	0

N.B.—The one Christian child in our series was admitted from the casualty room.

Temperature—In almost all the cases the temperature had been high at some time in the initial phase, even though it might not have been so at the time of hospitalisation. Table 6 gives the ranges of temperature at the time of admission.

TABLE 6—SHOWING DISTRIBUTION ACCORDING TO THE RANGE OF TEMPERATURE

Temperature	No. of cases
Up to 98·4°F ...	14
From 98·4° up to 100°F ...	36
Above 100° up to 103°F ...	173
Above 103° up to 106°F ...	75
Above 106°F	3
Total ...	301

The minimum temperature was 97°F in two cases. In one of them it went up and persisted as low grade pyrexia for a long period. This child developed extrapyramidal syndrome. In the other child who had aphasia with paralysis of left leg and right half of face, the temperature remained below normal throughout. The maximum temperature recorded was 109·6°F in one child who expired after a few hours.

One remarkable feature observed in these cases was the marked fluctuation in the temperature recorded at the casualty room or the out-patient's department as compared to that recorded in the wards. Temperature is not routinely recorded in all cases at the casualty room, but wherever such readings were available (111 cases), this sort of variation in the temperature was found to be present in a majority of cases (103 cases).

A hectic type of temperature was frequently observed in the initial phase of the illness. This usually settled to normal within a few days with clinical improvement (Table 7).

TABLE 7—SHOWING THE DURATION OF PYREXIA IN 189 CASES

Duration of pyrexia	No. of cases
Up to 24 hours ...	32
Between 1 and 2 days ...	52
Between 2 and 3 days ...	36
Between 3 and 4 days ...	20
Between 4 and 6 days ...	23
Between 6 and 8 days ...	11
Between 8 and 10 days ...	5
More than 10 days ...	10
Total ...	189

In three patients it took more than one month for the temperature to return to normal. All these cases had some form of neurological complications.

Pulse—The pulse rate in the majority of children corresponded with the temperature. The pulse was only informative in cases who developed peripheral vascular failure.

Blood pressure—In none of the cases the blood pressure was unusually high. A fair percentage of cases showed an unrecordable or a very low blood pressure. The development of peripheral vascular failure is of ominous significance. Many of these cases were put on noradrenaline drip, which brought the blood pressure back to normal, but these children soon succumbed to respiratory failure or pulmonary oedema.

Pulmonary signs—Approximately 10 per cent of cases (32 children) at the time of admission showed signs of bronchitis along with the typical picture of encephalitis. They recovered in due course. Forty-two cases (14 per cent approximately) had typical signs of pulmonary oedema at the time of admission whereas 16 cases developed it later on or terminally. Most of these cases were severely dyspnoeic, had cyanosis and frothing at mouth and nose, and eventually expired. Recurrent pulmonary oedema was also noticed in a few fatal cases.

NEUROLOGICAL FINDINGS :

(a) *Alteration in the state of consciousness*—Gross disturbances of consciousness were present in 166 cases (55·1 per cent). 110 cases (36·5 per cent) were in a deeply comatose condition out of which 56 subsequently expired. Fifty-six (18·6 per cent) cases were in a semiconscious state, 10 of which expired later on. Undue irritability was observed in 42 children, while 36 showed apathy, lethargy or drowsiness. Fifty-seven children did not show any definite change in their mental state. These observations are presented in Table 8, the figures in parentheses show the number of cases expired in the corresponding group.

TABLE 8—SHOWING THE NEUROLOGICAL CONDITION IN 301 PATIENTS

State	No. of cases	Per cent
Unconscious	110 (56)	36·5 (50·9)
Semiconscious	56 (10)	18·6 (17·8)
Lethargic	36 (2)	11·9 (5·5)
Unduly irritable	42 (3)	13·9 (7·1)
No change	57 —	18·9 —
Total ...	301 (71)	

N.B.—Figures in parentheses denote the number of cases expired.

(b) *Abnormal movements*—A variety of abnormal movements was observed. Not less than 51·8 per cent (156 cases) exhibited generalised convulsions after the onset of the disease, either before admission or in the hospital. In the severe form they were of tonic type, involving mainly the extensor group of muscles. These lasted from a few seconds to about 20 or 30 minutes and occurred with varying frequency in individual cases. The patients assumed various types of attitude depending upon the muscles predominantly involved. In other children they were less generalised, involving one or both limbs, on one or both the sides. Twisting of limbs, rolling up of eyeballs, passage of urine and stool, frothing from mouth and nose, grimacing, etc., were frequent accompaniments.

Yet another evidence of involvement of the encephalon was noticed in children in the form of involuntary movements of a bizarre nature. Some of these children showed rolling up of eyeballs, fluttering of single eyelid with a fixed gaze, twitching on one side of face without any other accompaniment, clonic contractions of fingers of one or both hands and plantar flexion of the foot on one side with or without a similar movement of toes. Peculiar katatonia-like attitudes were seen in some unconscious children characterised by holding up of one extremity in a state of extension accompanied by fist formations or plantar flexion of the foot.

(c) *Tremors and parkinsonian features*—Rigidity, tremors, attitude of flexion, conjugate ocular deviation and choreo-athetoid movements were noticed in different patients in varying combinations, though the number of children showing a typical parkinsonian picture was not high.

(d) *Cranial nerves*—As opposed to encephalitis lethargica, the affection of cranial nerves during the acute stage was seen in a small number of cases. Paralytic strabismus (6th nerve) was found in 4 cases and lower motor neurone type of unilateral facial palsy in two. Half of these children showed gradual improvement towards recovery during their stay in the hospital, while in the other half the symptoms persisted to more or less the same degree.

(e) *Pupillary reactions*—Variations in size and abnormal reactions of the pupils were observed in less than half of the total cases. The more serious type of cases gave a sluggish reaction to light, while fixed pupil signalled a grave prognosis. The findings are given in Table 9, the figures in parentheses show the number of fatal cases in the corresponding group.

TABLE 9—SHOWING PUPILLARY REACTIONS

Pupillary size and reaction	No. of cases	Per cent
Normal	166 (7)	55·1 (4·2)
Dilated and sluggish ...	92 (41)	30·5 (44·5)
Constricted and sluggish ...	18 (8)	5·9 (44·4)
Dilated and fixed ...	11 (7)	3·6 (63·6)
Constricted and fixed ...	11 (7)	3·6 (63·6)
Unequal with varying reactions	3 (1)	1·0 (33·3)
Total ...	301 (71)	

(f) *Motor system*—Paresis and paralysis of various parts of the body were seen in a number of cases, the lession being mostly of the upper motor neurone type. Only two cases showed flaccid paralysis, one of the leg and the other of the forearms. A majority of the cases with paralysis improved to a variable extent over a period of time (Table 10).

TABLE 10—SHOWING INCIDENCE OF PARESIS OR PARALYSIS IN 12 CASES

Lesion	No. of cases
Paralysis of right lower limb (U.M.N. type) ...	2
Flaccid paralysis of right lower limb ...	1
Right-sided hemiplegia	3
Left-sided hemiplegia	1
Right-sided hemiparesis	2
Paresis of both upper limbs	2
Paresis of all four limbs	1
Total ...	12

The other group of cases showed only disturbance of muscular tone. Muscular hypertonia in the form of rigidity of the limbs or trunk of varying degrees was found in 38 children. Of these 15 expired, 18 were discharged relieved, and the remaining 5 went into the group showing neurological sequelae. On the other hand, 11 children had generalised muscular flaccidity. All were in a deeply comatose state. In most of them reflex

activity was absent, and only a few cases gave a weak response to tendon jerks. In this group, only 3 cases recovered and the remaining 8 finally met a fatal end.

(g) *Signs of meningeal irritation*—Definite stiffness in the neck along with a positive Kernig's sign was found in 184 children (61·1 per cent). These findings were doubtful in another 22 cases (7·3 per cent). Of the former group, 62 expired, 115 were discharged relieved and only 7 remained with neurological sequelae.

(h) *Superficial reflexes*—About 50 per cent children showed the absence of superficial abdominal reflexes associated with various other neurological features. In children, the plantar reflex is usually taken with some scepticism, and Table 11 shows the significance of the presence of this sign with associated severity of condition of the patient and the final outcome. The figures in parentheses show the number of fatal cases in each group.

TABLE 11—SHOWING THE OUTCOME OF CASES WITH RESPONSES TO PLANTAR REFLEX

Age, with the state of consciousness	Plantar response				
	Bilateral extensor	Bilateral flexor	Absent	Equivocal	Varying on two sides
Less than 1 year, with coma ...	5	1	0	3	0
Less than 1 year, without coma ...	12	1	0	1	0
More than 1 year, with coma ...	82 (30)	8 (5)	21 (18)	4 (2)	6 (3)
More than 1 year, without coma ...	49 (3)	99 (1)	0	7	2

Most of the children over one year of age, who later on developed neurological sequelae, showed an extensor plantar response initially. From the same group one child showed a varying response on the two sides, while another aged 8 months exhibited a flexor response.

(i) *Deep tendon jerks*—The deep jerks were exaggerated in 107 (35·3 per cent), diminished in 40 (13·2 per cent), and absent in 30 (10 per cent) of patients. The last group also included most of the cases having generalised muscular flaccidity, who were obviously in a state of neurological shock. In a small number, however, the jerks were unequal on the two sides, and many of these cases had gross neurological signs of the nature of paresis and paralysis.

TABLE 12—SHOWING COMMON SYMPTOMS OBSERVED

Symptoms	No. of cases	Per cent
Fever	278	92·3
Convulsions	156	51·8
Vomiting	118	39·2
Unconsciousness	110	36·5
Conjugate ocular deviation ...	102	33·8
Tremors	98	32·5
Lethargy and drowsiness ...	86	28·6
Irritability and startling ...	64	21·3
Frothing	62	20·6
Semiconsciousness	56	18·6
Diarrhoea	54	17·9
Rigors and chills	54	17·9
Headache	20	6·6
Headache and vomiting ...	18	5·9
Body ache	12	3·9
Pain in abdomen	11	3·6
Delirium	11	3·6
Rigidity of limbs	7	2·3
Paralysis	7	2·3
Urinary incontinence ...	6	1·9
Constipation	4	1·3
Urinary retention	3	1·0
Inability to speak	3	1·0
Squint	3	1·0
Inability to swallow	3	1·0

TABLE 13—SHOWING COMMON SIGNS ELICITED

Signs	No. of cases	Per cent
Meningeal irritation	206	68·6
Convulsions	156	51·8
Absent abdominal reflexes ...	150	49·9
Extensor plantars	148	49·8
Flexor plantars	109	36·3
Unconsciousness	110	36·5
Exaggerated jerks	107	35·6
Dilated pupils	103	34·2
Tremors	98	32·5
Peripheral circulatory failure ...	74	26·6
Semiconsciousness	56	18·6
Absent corneal reflex	52	17·2
Sluggish jerks	40	13·1
Muscular hypertonia	38	12·5
Absent jerks	30	9·9
Constricted pupil	29	9·6
Muscular hypotonia	11	3·6
Paralysis	7	2·3
Parkinsonism	6	1·9
Paresis	5	1·6
Aphasia	5	1·6
Strabismus	4	1·3
Facial palsy	2	0·6
Nasal regurgitation	1	0·3
Rashes (urticarial)	1	0·3

(j) *Organic reflexes*—It was difficult to assess the integrity of the sphincters in the very ill and

convulsive patient and in those who were indeed very young. Deranged functions were seen in a very small number of cases in the form of retention (1 per cent) or incontinence (2 per cent) of urine all of whom had a normal bladder control previously. None of them showed any signs of cord lesion.

SYMPTOMS AND SIGNS :

The common symptoms and signs are given in Tables 12 and 13 respectively.

INVESTIGATIONS

Total leucocytic count—The total leucocytic count of 243 children is summarised in Table 14 in round figures. The lowest count obtained was 2,550 cells/c.mm and the highest 40,500/c.mm.

TABLE 14—SHOWING THE TOTAL LEUCOCYTIC COUNT

Leucocytes/c.mm. in range of round figures	No. of cases
2,000 to 4,000	5
5,000 to 7,000	25
8,000 to 9,500	41
9,600 to 12,000	102
13,000 to 18,000	51
19,000 to 30,000	16
31,000 to 40,000	3

Differential leucocytic count—Polymorphonuclear leucocytosis, up to 96 per cent, was seen in 65 per cent children. The lymphocytes were increased in 10 per cent. In a small number of cases eosinophilia upto 26 per cent was met with.

Blood sugar—Fasting blood sugar levels were analysed in 101 cases. The observations are given in Table 15.

TABLE 15—SHOWING BLOOD SUGAR LEVELS

Blood sugar in mg./100 c.c.	No. of cases
18 (lowest)	1
20 to 50	20
51 to 80	29
81 to 120	31
121 to 150	13
151 to 200	6
240 (highest)	1

Cerebrospinal fluid—The C.S.F. obtained from lumbar puncture was uniformly clear and invariably under tension. The cell counts and results of biochemical analysis of the C.S.F. are given in Tables 16 to 19.

TABLE 16—SHOWING C.S.F. CELL COUNT

No./c.mm.	No. of cases
Up to 5	120
6 to 10	22
11 to 20	15
21 to 50	5
62	1
Total	163

TABLE 17—SHOWING C.S.F. PROTEINS

Proteins mg./100 c.c.	No. of cases
10	7
15 to 40	180
41 to 50	4
51 to 100	5
101 to 200	2
Total	198

TABLE 18—SHOWING C.S.F. SUGAR

Sugar mg./100 c.c.	No. of cases
10 to 50	46
51 to 90	141
91 to 120	12
135	1
Total	200

TABLE 19—SHOWING C.S.F. CHLORIDES

Chlorides mg./100 c.c.	No. of cases
440 to 670	37
680 to 750	140
760 to 780	9
Total	186

CLINICAL COURSE

A close observation of the hospitalised patients in the first few weeks made it quite apparent that we were dealing with at least three types of cases with different clinical courses. Looking at the onset it was well-nigh impossible to predict as to which patient was going to take a particular course. Different classifications have been put for-

ward by various authors, based either on the severity of illness, the pattern of the temperature curve, or on the ultimate outcome of recovery or mortality. None of them have taken into account the composite clinical picture and the likely behaviour of the underlying causative agent. Following is the proposed classification drawn up on the basis of the clinical course observed in the hospital and on follow-up.

I. *Acute*—(1) With fulminating course leading to death, (2) With neurological signs and complete recovery, (3) With neurological sequelae, and (4) Suspected abortive cases.

II. *Subacute or chronic*—Showing evidence of a progressive or changing neurological picture with persistent or recurring low-grade pyrexia.

III. *Relapsing*—with acute attacks occurring at least twice with an apyrexial phase of one or more days (in the majority 1 to 3 days) when the children apparently looked well. These cases were again subdivided as in the acute group.

I. ACUTE:

1. *Fulminating course leading to death*—There were in all 71 cases who expired in the hospital. The characteristic features in this group were a sudden onset, a short, stormy course with signs of acute involvement of the encephalon and its meninges and a moderate to marked leucocytosis in peripheral blood with polynucleosis. Circulatory failure as indicated by a sinking blood pressure, a rapid thready pulse and pulmonary oedema usually preceded the fatal end.

CASE REPORT

B., 2 years, Muslim, female child, got fever on the morning of 2-8-1958 followed quickly by paroxysms of generalised tonic convulsions, and the temperature rising steadily within a few hours. The child became delirious and unconscious. Later on the convulsions were seen more marked on the left side of the body.

On examination—Pulse 120/min., B.P. 96/60, tachypnoea and frothing from nose and mouth present, bilateral basal pulmonary congestion +, pupils widely dilated and fixed. C.N.S.—Unconscious, no response to painful stimuli; one-sided convulsions +, neck rigidity ++, Kernig's sign +. Superficial reflexes absent, deep tendon jerks exaggerated.

Investigations—W.B.C. 14,000 cells/c.mm. Diff. count—Polymorphs 75 per cent, lymphocytes 23 per cent, monocyte 1 per cent, eosinophil 1 per cent. C.S.F.—Tension ++, cells less than 5/c.mm., proteins—20 mg. per cent, sugar—60 mg. per cent, chlorides—690 mg. per cent. Culture—sterile. Fasting blood sugar—84 mg. per cent. Clot culture—Sterile. Urine—Normal. Fundus—N.A.D.

Glucose and noradrenaline by I.V. drip was given together with other therapeutic measures but the condition rapidly went downhill. Marked pulmonary oedema and peripheral circulatory failure were seen in the terminal phase. Total duration of illness was 55 hours.

2. *With neurological signs and complete recovery*—Out of the 98 children in this group, 48 showed signs of diffuse involvement of the encephalon, while in the other 50 the brunt fell on some localised regions, manifested by localised convulsions, monoplegias, hemiplegias, aphasia, unilateral Babinski's signs, etc. The sudden onset and the acute course was similar to that observed in the fatal group of cases. Subsequent events were unpredictable. The essential difference between the two groups was that in the fatal group all the children expired whereas in this group, although looking ill, toxic and moribund, they survived and showed no residual lesions.

3. *With neurological sequelae*—The neurological signs, as observed in the preceding group, did not disappear in this group of cases (4 only) after the critical phase was over. A high temperature, unconsciousness, convulsions, and other signs of acute inflammation of the brain lasted but for a few days, to leave different types of neurological sequelae, viz., rigidity, squint and lower motor neurone type of paralysis.

CASE REPORT

B.M., 1½ year, Hindu, male child, became restless in the early hours of morning of 15-7-1958 and was found to be having fever which rapidly shot up to 104°F. Rolling up of eyeballs, and startling were followed by rigidity of the whole body punctuated with paroxysms of convulsions. The child rapidly became unconscious. The convulsions and unconsciousness disappeared in two days, the fever lasting for another couple of days. The rigidity however persisted.

On examination—Pulse 130/min., B.P. 98/66. Axillary temperature normal at time of admission. C.N.S.—Fully conscious but apathetic, all limbs hypertonic and held in a state of semiflexion and inward rotation. Deep tendon jerks brisk, plantar reflexes flexor.

Investigations—W.B.C.—13,000/c.mm., Diff. count—Polymorphs 70 cent, leucocytes 30 per cent, C.S.F.—Tension +, cells less than 10/c.mm. proteins—30 mg. per cent, sugar—65 mg. per cent, chlorides—710 mg. per cent. Culture—Sterile. Fasting blood sugar—200 mg. per cent. Fundus—N.A.D. The condition later remained more or less stationary. Later, the mental attitude improved, but the extrapyramidal type of rigidity persisted.

4. *Suspected abortive cases*—In 60 children, no significant neurological signs could be elicited, though all of them had an onset identical with cases described in the other groups. Sudden high pyrexia, convulsions, restlessness, lethargy, un-

consciousness, headache, vomiting, bodyache, loose motions—any one or more of these symptoms were conspicuous, to which no tentative cause could be ascribed after thorough clinical and laboratory investigations.

Case Report

G.P., 4 years, Hindu, male child, while playing in the evening felt giddy and weak. The temperature rapidly became high and within 15 minutes convulsions started and the child became unconscious. After about 3/4 hr. he came round but remained lethargic and drowsy.

On examination—Pulse 128/min., respiration 32/min., temperature 102°F (axillary). Pupils and throat normal. Examination did not reveal any abnormalities in gastro-intestinal, respiratory, circulatory or nervous systems.

Investigations—W.B.C. 10,500/c.mm., Diff. count—Polymorphs 74 per cent, leucocytes 24 per cent, eosinophil 1 per cent, monocyte 1 per cent. Blood sugar 90 mg. per cent; C.S.F. normal; Urine normal. Blood film for M.P.—negative. Subsequently the temperature touched normal after 36 hours. The child remained a little weak for a couple of days after which he was discharged cured. He continued to be normal till the last follow-up 6 months later.

II. SUBACUTE AND CHRONIC:

This group comprising of 15 children was characterised by a protracted course, accompanied by a low grade, undulating course of temperature and essentially showing a changing neurological picture, ultimately making the patient more or less an invalid, mentally or physically or both. Various types of lesions were seen, viz., cranial nerve palsies, hemiplegias, other paralyses as well as post-encephalitic extrapyramidal syndrome. After a prolonged observation of such patients it appeared that the causative agent after producing damage of particular regions in brain, remained smouldering in the tissues for a long time and was thus responsible for the characteristic clinical picture taking a subacute or chronic course. Out of 15 cases included in this group, 8 showed the involvement of the extrapyramidal system; one, of the pyramidal system resulting in left-sided hemiplegia; and one of combined pyramidal and extrapyramidal systems, resulting in hemiplegia and tremors along with aphasia, squint and mental disorientation.

Case Report

G., 3 years, Hindu, male child, got sudden high fever accompanied by a few vomits. Soon he lost his speech, the body became rigid, eyeballs rolled upwards and he started having convulsions all over the body followed by unconsciousness. For three days he was treated at a district hospital without any improvement. In this period he also passed loose, yellowish, foul-smelling stools, about 15-20 per day.

On examination—The child looked very ill and toxic, temperature 105°F, respiration 32/min., pulse 112/min. Pupils dilated and sluggishly reacting to light. C.N.S.—unconscious, rigidity all over the body, lying with a hyperextended spine and flexed limbs and an attitude of torsion dystonia. No response was shown to painful stimuli. Deep tendon jerks were exaggerated. Plantars bilaterally extensor. Neck rigidity +, Kernig's sign +. Intermittently he showed generalised tonic convulsions lasting for a few minutes. Oral tendencies* and choreo-athetoid movements were also observed.

Investigations—W.B.C. 5,200/c.mm. Diff. count—Polymorphs 56 per cent, lymphocytes 36 per cent, eosinophil 1 per cent and monocytes 7 per cent. C.S.F. was normal, except tension +++. Urine N.A.D.

III. RELAPSING TYPE:

This type included 53 cases. Out of these, 23 children sought admission to the hospital for a second time, after a variable asymptomatic period. The second admission was made 3 days to 1½ months after the initial admission. The remaining 30 patients during their stay in the hospital showed a relapsing picture, as characterised by recurrent episodes of rise in temperature above 100°F, with or without abnormal neurological findings. The asymptomatic intervals in between the successive events varied in most of the cases from 2 to 6 days. The clinical picture during relapses conformed to the acute type, as described above. Table 20 shows the number of cases of this group as classified above.

Table 20—Showing the Number of Cases in the Relapsing Type

Type of relapse	No. of cases
Acute fulminating relapses leading to death	2
Acute relapses with generalised neurological signs and complete recovery ...	13
Acute relapses with focal neurological signs and complete recovery	17
Acute relapses with neurological sequelae ...	1
Suspected abortive relapses	20
Total ...	53

Discussion

For nearly half a century in the past, there had been outbreaks in various parts of the world, of acute infections of the C.N.S., apart from polio-

* The authors purposely use the comprehensive term for clicking of the tongue, smacking of lips, grimacing, biting, putting fingers, thumb or even the fist in the mouth to a grossly abnormal extent.

myelitis and meningitis. Clinical and laboratory data accumulating during this time, indicated that such epidemics were due to acute encephalitis. Though the disease existed for a long time, the first classical description in the literature was by von Economo who described an epidemic of encephalitis lethargica in 1917.

Of the various aetiological agents, viz, physical, chemical and bacterial, viruses are now incriminated as being responsible for many of the severe epidemics occurring in different countries of the world. It is customary to designate the disease by the name of the place of its occurrence, e.g., St. Louis, Japanese B, Russian spring-summer, Murray Valley, West Nile, Venezuelan equine, Australian X disease, Jamshedpur fever, Kyasanur forest disease, etc. In many of the above, the causative factor, a virus, has been isolated. For different entities, different viruses have been held responsible and on some occasions antigenic variants of the same virus have produced unidentical clinical syndromes. The serological relationship between the viruses of St. Louis, Japanese B, and Russian spring-summer complex is already known (Rivers, 1958). In India, the virus of Kyasanur forest disease has been found to be serologically identical with Russian spring-summer complex virus (Work *et al*, 1957), and that of North Arcot encephalitis (Webb and Pereira, 1956) to the Japanese B encephalitis virus (Work *et al*, 1956). Out of many outbreaks in this country and abroad, viruses have been presumed to be the causative agents, for lack of any other convincing aetiologic agents.

The first major epidemic in India broke out in 1954 at Jamshedpur followed successively in many parts of Northern India during the subsequent months (Khan, 1954 ; Swami and Chari, 1955 ; Seal and Ghose Chowdhury, 1956 ; Taneja, 1955 ; Gour, 1956). The common denominator in these epidemic outbreaks has been an acute febrile illness, occurring explosively, affecting mainly children, showing in most of the cases features of involvement of the encephalon, a high mortality rate, with a variable incidence of neurological residue among the survivors. As a clinical syndrome it has to be accepted, although the mystery about its aetiological agent remains. Research workers will only be happy when such an agent is isolated, as happened in the various western encephalitides. The only fact that can be categorically stated now is that it is a definite clinical entity of great import, similar to many conditions of dubious aetiology, such as encephalitis lethargica, infectious mononucleosis, etc.

In this study, we had 319 cases initially admitted with the provisional label of acute epidemic encephalitis, out of which 18 cases were subsequently discarded because a convincing alternative diagnosis could be reached in them.

The clinical picture in this epidemic was remarkably uniform. Most of the cases showed an abrupt onset, high pyrexia, varying degree of loss of consciousness, different types of convulsions, a variegated assortment of focal or general neurological findings, a good number of residual sequelae and a high mortality rate. Investigations in the majority of instances revealed a more or less normal C.S.F., and a leucocytosis in the peripheral blood, with a relative increase of polymorphs. All types of blood sugar levels were found, varying from hyperglycaemia to hypoglycaemia, a larger proportion of cases showing the latter. A host of other investigations, viz., liver function tests, serum proteins, clot culture, liver biopsy, etc., did not show any significant abnormality. In some cases the virological studies showed the evidence of a cytopathogenic agent, which has been discussed in a separate paper (Gupta *et al*, 1959)

The clinical features of severe cases of different varieties of encephalitis are too dramatic and arresting to escape notice. Mild cases of encephalitis do occur which would otherwise have been missed, but for the positive virological and serological investigations as exemplified by a percentage of cases of St. Louis encephalitis (Muckenfuss *et al*, 1934 ; Hempelmann, 1934). In the present series, we included 60 cases which were regarded as suspected abortive cases of encephalitis, even though they did not show any typical signs of encephalon involvement. All of them had an identical abrupt onset, with startling, vomiting, hyperpyrexia, toxaemia, just as the cases with the neurological sequelae or the fatal cases had. No other definite diagnostic label could be given to these cases. Since they were seen in the phase of epidemic, they were included in this series. A few of these abortive cases subsequently relapsed after a variable interval showing definite neurological signs. This group has been considered together with other cases of the relapsing variety. As proved abortive cases are common in other encephalitides and in poliomyelitis, there seems to be every justification for their inclusion, unless otherwise disproved by negative virological and serological findings.

Although the cause is not known, there is a fairly definite clinical pattern of the condition which prompted us to investigate the epidemic on the lines of an infection. Sporadic cases with identical clinical picture to the present series were admitted in Children's Hospital throughout the

year, and the occurrence of the epidemic during the summer months strongly suggested an infective nature. The occurrence of fulminant cases in the early part and less fulminant and abortive cases in the later phase, its predilection for infants and children, the suspicion of multiple cases occurring in a fair percentage of families affected, the finding of polymorphonuclear leucocytosis, and the fact that all the cases had high pyrexia at some stage or the other are strong pointers towards such an aetiology.

No bacterial, protozoal or metazoal agent could be discovered in spite of intensive laboratory search and the consensus of opinions today favours the causative agent to be a virus. There are other supporting evidences also which indicate that a virus may be at work, e.g., selection of relatively healthy children, presence of leucocytosis in peripheral blood and failure of any significant response to antibiotics. The exact nature of the virus, however, cannot be stated at the present time, as the virological investigations are not yet complete. The occurrence of sporadic cases throughout the year and the seasonal incidence of epidemic outbursts, easily attracts attention and leads us to suspect the endemic nature of the disease with epidemic outbreaks.

The clinical picture of various epidemics in India show broad points of similarity, e.g., sudden febrile onset with hyperpyrexia in a high percentage of cases, rapid course of the disease in some, the evidence of encephalon involvement in a large number, failure to demonstrate bacterial, protozoal or metazoal infection, and finally the raised C.S.F. tension along with the absence of any other definite C.S.F. abnormality. The odd findings of high C.S.F. sugar values and hyperglycaemia in our series are similar to the observations made in Delhi, Agra, and Jamshedpur cases. These raised sugar values had not been reported in the St. Louis and Japanese Type B encephalitides.

In the present series 66·7 per cent of children were between 1 and 5 years of age, a figure comparable to the Nagpur (69·6 per cent) and Agra (67·7 per cent) epidemics but significantly different from Jamshedpur where the incidence in comparable age groups was much lower (Taneja *et al*, 1954 ; Berry *et al*, 1959 ; Mathur and Prasad 1959 ; Seal and Ghose Choudhury, 1956). The uniform increase in white blood cells with a polymorphonuclear preponderance and a relatively normal C.S.F. finding are in keeping with the reports of other Indian authors.

The mortality rate in the present series was 23·5 per cent in the acute phase as opposed to the Delhi epidemic (56·1 per cent) and in Jamshedpur cases (13·5 per cent) (Taneja *et al*, 1954 ; Seal and Ghosh Chowdhury, 1956), perhaps because the suspected abortive cases were excluded in the Delhi series, whereas in Jamshedpur, adults constituted 47·5 per cent of the whole series, all of whom except two survived. The mortality rate at Jamshedpur would be comparable to the present series if the adult cases were excluded.

At first sight one may be tempted to explain away many of the symptoms on the basis of a hypothalamic dysfunction, but it seems to be unlikely considering that none of the affected cases showed the evidence of classical symptoms of hypothalamic involvement, like polydypsia, obesity and disturbances of sleep rhythm. We think that symptoms like high swinging temperature, hypoglycaemia, vomiting, pulmonary oedema and peripheral vascular failure, can more justifiably be explained on the basis of viraemia and its associated toxaemia. Such a viraemia is now regarded as a regular feature in virus infections before localisation takes place in the organs. As far as the affection of the nervous system is concerned it appears that the virus has a predilection for the basal ganglia, as shown by the characteristic neurological sequelae, viz., choreo-athetoid movements, extrapyramidal rigidity and torsion of the body. Cases who showed extrapyramidal involvement were almost invariably accompanied by a damage of the higher cortical centres, like personality changes, loss of contact with the surroundings, aphasia, deafness, etc. Some of these cases later on remained mentally deficient, even though the extrapyramidal signs showed regression.

Summary

1. 301 cases of acute epidemic encephalitis occurring at Lucknow in July, August, and September, 1958, are reported.

2. The epidemiology, clinical features with special mention of neurological involvement and laboratory investigations are discussed.

3. A new classification of this condition has been proposed on the basis of the clinical course in the hospital and on follow-up.

4. The aetiology and pathogenesis of the epidemic have been discussed.

Acknowledgments

We are grateful to Prof. V. S. Mangalik, Principal, King George's Medical College, Lucknow, for his keen interest and guidance at every stage of this work, without whose help an epidemic of such a magnitude could not have been handled and studied. We are also grateful to Dr. T. D. Shahani, former Superintendent, G. M.

and Associated Hospitals, Lucknow, for providing extra facilities during the epidemic phase and for permitting the use of the case material. We are indebted to Prof. B. B. Bhatia, Prof. S. S. Misra and Dr. K. B. Kunwar for their kind guidance and helpful criticisms. Our thanks are due to the State authorities, particularly to Dr. K. M. Lal, Diretor, Medical and Health Services, U. P., Lucknow, who extended generous help at every stage of the epidemic. We indeed appreciate the interest evinced by the I.C.M.R. and the timely visit of Dr. C. D. Pandit and Dr. T. H. Work which gave a new impetus to the work. We are grateful to Dr. A. S. Siddhu, I.C.M.R. scholar, for providing the opportunity to compare notes at first hand. We are also thankful to Drs. J. K. Agarwal, S. K. Goel, Malti Sharma, the resident staff, postgraduates and the nursing staff without whose help this study could not have been possible.

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HAEMOGLOBIN E DISEASE IN BENGALEES

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The distribution of haemoglobins C, S and E as reported so far appears to have some sort of racial and geographic predilection. Haemoglobin C has been reported mostly in Negro population. Haemoglobin S is also found predominantly in people of Negroid ancestry, though scattered foci in non-negro population have been found in India, Middle East and Mediterranean countries. Haemoglobin E has been reported almost exclusively from south-eastern Asian countries, its incidence being as high as 15·3 per cent in Burma (Lehmann, Story and Thein, 1956). It has been reported to the extent of 13·6 per cent in Thailand (Na-Nakorn, Minnich and Chernoff, 1956), 7·3 per cent in Malaya (Lehmann and Singh, 1956) and 3 to 13 per cent in Indonesian islands (Lie-Injo Luan Eng, 1959). In Malays, Vella and Raman (1959) have recorded an incidence of 6·3 per cent in Malays and 0·43 per cent in Chinese population. In Ceylon, haemoglobin E has been found not only in Veddas but also in Sinhalese (de Silva, Jonxis and Wickramasinghe, 1959). In India, haemoglobin E has been found in 3·9 per cent of the Bengali population (Chatterjea, Swarup, Ghosh and Ray, 1957); instances of haemoglobin E have also been encountered among the Assamese and Nepalese (Chatterjea, 1957). We have also detected haemoglobin E in blood samples of a Jat Sikh family from Patiala and one Tamil family from Madras. Occasional instances of haemoglobin E have, however, been reported from Turkey, Persia and Philippines (Lehmann, 1959).

Haemoglobin E has been found in heterozygous or homozygous form or in combination with thalassaemia. The heterozygous form is asymptomatic, the homozygous form (haemoglobin E disease) contributory to mild anaemia, while interaction with thalassaemia gene usually gives rise to severe anaemia (Chatterjea *et al*, 1956; Chernoff *et al*, 1956; Lie-Injo Luan Eng, 1959). Instances of haemoglobin E have further been recorded in association with haemoglobin S (Aksoy and Lehmann, 1957) and haemoglobin K (Haematological Research, 1960).

We have so far encountered 5 instances of homozygous E (haemoglobin E disease). Detailed study has been done on three of these cases and is reported in the present communication.

Material and Methods

The group of three subjects reported herein was encountered during investigation of patients with the thalassaemia syndrome. Two patients were the mothers of patients with haemoglobin E-thalassaemia disease while the third was referred as a case of refractory anaemia with leukaemoid blood picture.

In addition to the routine clinical and haematological examinations, the following investigations were carried out:

1. Osmotic fragility of red cells in graded hypotonic saline solutions.
2. Electrophoresis of haemoglobin according to the techniques already reported (Chatterjea, Saha, Ray and Ghosh, 1956).
3. Sickling test according to the method of Daland and Castle (1948).
4. Foetal haemoglobin estimated by the method of Singer, Chernoff and Singer (1951).
5. Therapeutic trial with iron and other haematinics.

Observations

Clinical examination revealed slight pallor and anaemia. One of the subjects (G.M.) showed slight icteric tinge in the conjunctivae. The spleen was not palpable in any while the liver was palpable in one (A.K.H.) to the extent of 3 cm. below the left costal arch. Details of haematological findings and other relevant data are shown in Table 1.

Electrophoresis of haemolysate of blood from each case showed a single peak in the position of E.

Sickling test was repeatedly negative in all the cases.

The percentage of alkali resistent haemoglobin was 0·86, 9·6 and 1·37 respectively.

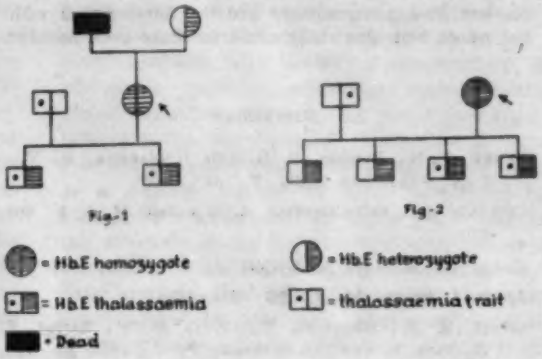
Treatment with haematinics (iron, folic acid and liver extract) did not improve the blood picture.

Family Study

Family of A. K. H.—The mother of the propositus was found to be haemoglobin E heterozygote. The other members were not available for examination.

Family of S. M.—The mother of S. M. was found to be heterozygote for haemoglobin E. The father had died of old age some years ago. The patient had two children (sons) both of whom were also found to be suffering from haemoglobin E-thalassaemia disease. The thalassaemia gene was inherited from the husband (Fig. 1).

Family of G. M.—G. M. had four children (sons). Two of these were haemoglobin E heterozygotes and the remaining two were cases of haemoglobin E-thalassaemia. Parents of the subject were, however, not available (Fig. 2).



Discussion

Instances of haemoglobin E disease have been reported from Thailand (Chernoff *et al*, 1956; Na-Nakorn and Minnich, 1957), Burma (Lehmann *et al*, 1956) and India (Chatterjea *et al*, 1957). The confirmatory family studies were, however, completed in only some of these cases. Na-Nakorn and Minnich (1957) reported hepatic enlargement in only two out of five otherwise symptomless cases of haemoglobin E disease. Blood picture was found to be microcytic and normochromic with a large number of target cells (61-79 per cent). Foetal haemoglobin was within normal limits (0·1-1·3 per cent). In the report from Indonesia by Lie-Injo Luan Eng (1959), the spleen was enlarged in three, and the liver in 2 out of 5 cases. Slight anaemia was reported in one case. Peripheral blood picture was microcytic and normochromic. Target cells were increased in 2 cases while in the remaining one only a few target cells were found. Normal level of alkali resistant haemoglobin was found in two cases and increased up to 6·4 per cent in the remaining 3 cases. In the cases reported in the present communication, easy fatiguability was a common complaint and mild anaemia a common finding. The spleen was not palpable in any case while the liver was palpable only in one subject (A.K.H.).

Slight icteric tinge was seen in one (G.M.). The blood picture was normocytic and normochromic. Target cells formed 10·4, 9·0, and 13·4 per cent of the total red cell population. Bilirubin content of the serum was 0·4, 0·2 and 0·8 mg. per cent respectively. Haemoglobin E was found to constitute 99·14, 90·4 and 98·63 per cent respectively of the total, the remaining being contributed by alkali resistant haemoglobin (0·86, 9·6 and 1·37 per cent respectively). On paper electrophoresis, a single peak in the position of E was detected in all the cases. Complete family study was not possible. Two patients transmitted haemoglobin E to all of their children so that each child was heterozygote for haemoglobin E. Fathers of these children were homozygotes for haemoglobin A.

Haemoglobin E-thalassaemia disease with a high proportion of haemoglobin E (Hb. 90 per cent) and haemoglobin F (10 per cent) may present an electrophoretic pattern of haemoglobin similar to that of haemoglobin E disease. The two conditions, haemoglobin E-thalassaemia and haemoglobin E disease, can only be clearly differentiated by family studies. An average case of haemoglobin E-thalassaemia disease is relatively more anaemic with overt signs of haemolysis. The differential diagnosis between haemoglobin E-thalassaemia and haemoglobin E disease is comparable to differential diagnosis between sickle cell anaemia and haemoglobin S-thalassaemia (Chatterjea *et al*, 1958).

Compared to the homozygous forms of haemoglobin S and thalassaemia, homozygous haemoglobin E is a milder condition. Homozygous forms of haemoglobin C (Singer *et al*, 1954, Diggs *et al*, 1954) and D (Chernoff, 1958) are probably milder still.

TABLE 1—SHOWING DETAILS OF 3 CASES WITH HAEMOGLOBIN E DISEASE

Serial No.	1	2	3
Name	A.K.H.	S.M.	G.M.
Age (years)	8	19	27
Sex	M	F	F
Splenic enlargement ...	0	0	0
Hepatic enlargement ...	3 cm.	0	0
Hb.(g. %)	10·4	10·1	9·2
R.B.C. in million/c.mm.	3·5	3·15	—
Ret. (%)	1·4	1·5	0·6
P.C.V. (%)	33	28	29
M.C.V. $c\mu\mu$	95	80	—
M.C.H. $\gamma\gamma$	30	29	—
M.C.H.C. (%) ...	32	37	32
Red cell morphology ...	Aniso + Poik +	Aniso + Poik +	Aniso + Poik +
Total nucleated cell count/c.mm. ...	13,600	6,800	7,200
Normoblasts/100 W.B.C.	2	Occasional	0
Serum bilirubin (mg/%)	0·4	0·2	0·8
Osmotic fragility ...	0·46-0·12	0·36-0·2	0·4-0·22
Electrophoretic pattern of Hb. ...	EE	EE	EE
Hb. E	99·14	90·4	98·63
Hb. F	0·86	9·6	1·37
Sickling test	Neg.	Neg.	Neg.

Compared to the homozygous forms of haemoglobin S and thalassaemia, homozygous haemoglobin E is a milder condition. Homozygous forms of haemoglobin C (Singer *et al*, 1954, Diggs *et al*, 1954) and D (Chernoff, 1958) are probably milder still.

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RARER CAUSES OF COR PULMONALE*

(Report of Two Cases)

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Introduction

Recent studies have uncovered certain rarer causes of cor pulmonale like repeated pulmonary embolism and primary pulmonary hypertension which need serious consideration, particularly in cases where clinical and radiological evidences of emphysema and pulmonary fibrosis are lacking and who present with comparatively short history and rapidly downhill course. With the widespread application of cardiac catheterisation more and more cases of primary pulmonary hypertension have been encountered and reported but cor pulmonale secondary to repeated pulmonary embolism has been recognised less frequently. The actual incidence of these two conditions can be established only when a large number of clinically diagnosed cases come to autopsy. Out of 111 autopsies that Mckeown (1952) performed on cases of cor pulmonale, he reported five cases of repeated pulmonary embolism and eight cases of primary pulmonary hypertension. In our country, as more autopsies are not frequently done, the exact incidence of these two conditions is difficult to be assessed. Out of fourteen autopsies performed during the last 3 years in this hospital on cases of cor pulmonale, we could record only one case of primary pulmonary hypertension and one case of repeated pulmonary embolism. In this paper, these two cases are briefly reported and the available literature on the subject discussed.

Primary Pulmonary Hypertension

Primary pulmonary hypertension is an entity of obscure pathogenesis. Its clinical diagnosis is made only by excluding the known causes of pulmonary hypertension. The final diagnosis on surer footings can be made only on autopsy.

The disease has been described in the age group between twenty and forty years. Sixty per cent of the cases are females. The disease usually runs a progressive downhill course of from 5 months to 5 years, characterised by right heart failure and terminating in sudden death. Clinical features consist of exertional dyspnoea, chest pain, syncope, palpitation, orthopnoea and haemoptysis. Besides clinical, radiologic and electrocardiographic evidences of pulmonary hypertension, clinical examination may also reveal systolic murmurs in mitral and pulmonary areas.

Pathology—Anatomical abnormalities in the heart and lungs that characterise primary pulmonary hypertension are hypertrophy and dilatation of right ventricle, dilatation of tricuspid ring, right auricular hypertrophy, dilatation of pulmonary valve and main pulmonary arteries with pulmonary atheroma and specific changes in the small pulmonary vessels. None of these anatomical abnormalities is pathognomonic of idiopathic pulmonary hypertension, since all may occur when severe pulmonary hypertension complicates cases with a left to right shunt.

Pathological studies have shown great variability of the lesion. Atherosclerosis is common in major arteries, particularly in the older subjects and is regarded as a secondary change. It is in small arteries and arterioles that most significant changes are found. These include fibro-elastic thickening of intima and hypertrophy of media, but normal vessels are nearly always seen. Evans *et al* (1957) reported one case with no histological evidence of vascular disease although arteriogram showed diffuse narrowing of smaller arterioles to half their normal calibre. Gilmour and Evans (1946) described hypoplasia of the media of many small vessels, which they believed was congenital in origin and found that endarteritis fibrosa was closely related and presumably secondary to the defect.

Pathogenesis of this disorder is, as yet, obscure. Although many theories have been put forward to explain the mechanism of pulmonary hypertension in these cases, the final answer is yet to come.

The disease usually runs a malignant course after the onset of congestive heart failure, and death usually occurs within 2 years. No treatment that has any significant influence on the course of the disease, has been described.

Illustrative Case

Case 1 (*Final diagnosis*: *Cor pulmonale secondary to primary pulmonary hypertension*)—An eighteen year old male was admitted to the hospital complaining of breathlessness and cough since the age of ten years, distension of abdomen after meals and constipation since

* Presented at joint annual conference of the Association of Physicians, Paediatricians, Cardiologists and Neurologists of India, New Delhi, January, 1960.

the age of 11 years and pain around right shoulder and right superior extremity since the age of 14. He also gave history of recurrent attacks of sore throat in the past. There was no history of chronic cough with or without expectoration or haemoptysis. He also denied any past history of rheumatic fever.

Physical examination at the time of admission revealed that the patient was dyspnoeic and the neck veins were engorged. There was oedema of the feet and the liver was palpable and tender. Tonsils were enlarged. B.P. was 100/42 mm. Hg. Pulse was 100/minute and regular. Temperature was 98·5°F. Examination of the cardiovascular system revealed a diffuse cardiac impulse with marked right ventricular heave. In the mitral area, the first sound was accentuated and there was a soft systolic murmur. Pulmonary second sound was accentuated. Respiratory and nervous systems were normal. Blood examination revealed slight leucocytosis. E.S.R. was 0 mm. for the first hour. E.C.G. showed right ventricular hypertrophy and strain. There was no evidence of auricular hypertrophy. X-ray of the chest revealed prominent pulmonary conus with normal intrapulmonary vascular markings.

The patient was kept on anticongestive heart failure measures without any improvement. One day he suddenly developed pain in the abdomen, urgency for defaecation with dyspnoea, and died.

Autopsy was performed. Heart was found to be enlarged and there was right ventricular hypertrophy and dilatation. Valves were found to be normal. Gross examination of the lungs was normal. Microscopic study revealed pulmonary atherosclerosis, otherwise pulmonary blood vessels were normal. Pathological diagnosis of pulmonary atherosclerosis leading to pulmonary hypertension and right heart failure was made.

Comments—With the clinical, radiological and electrocardiographic findings, the diagnosis of pulmonary hypertension was made. Conditions like chronic bronchitis with emphysema and common congenital heart diseases like atrial septal defect, ventricular septal defect and patent ductus arteriosus were excluded on clinical grounds. In view of the young age of the patient and recurrent attacks of sore throat, the diagnosis of mitral stenosis was entertained, but could not be considered due to lack of left auricular enlargement and the absence of definite diastolic murmur in the mitral area. However, final diagnosis could be established only after the death of the patient. Autopsy findings excluded the possibility of any lung disease or any heart disease, congenital or acquired, to account for pulmonary hypertension. In the absence of any other lung or cardiac pathology and due to presence of pulmonary atherosclerosis, the diagnosis of primary pulmonary hypertension was finally made.

Repeated Pulmonary Embolism

Cor pulmonale secondary to repeated pulmonary embolism is now a well recognised entity and should be suspected in all cases of congestive heart failure associated with pregnancy or thrombophlebitis of leg veins particularly in the absence of any cardiac or parenchymal lung disease.

The pathogenesis of this condition has now been clearly understood. The embolus is usually derived from the thrombus in pelvic or leg veins, although cases are on record where it was derived from thrombophlebitis following an infection in hand and thrombosis of portal vein (Mantz and Craige, 1951). Owen *et al* (1953) described two cases where emboli arose within the heart. The embolus derived from any of these sites finally gets impacted into pulmonary arteries, the effect of which depends on the size of the vessel which is blocked—large vessel occlusions are followed by infarction of the lung distal to obstruction. Studies have shown that thrombosis frequently complicates embolism and then it may be difficult to identify the underlying embolus particularly if the clot is partially organised.

Pathogenesis—It has been noted that due to repeated emboli, the pulmonary artery pressure becomes permanently raised which in its turn, not only initiates vasoconstriction in the pulmonary vascular bed but also produces initial proliferation in smaller vessels, thereby producing increasing obstruction to pulmonary blood flow. The combination of all these factors leads to sustained pulmonary hypertension which ultimately leads to right heart failure.

This disease usually runs a downhill course. Intensive treatment in early cases may be of value, hence early diagnosis is important. Primary site of origin of embolus must be treated by ligation of the main veins. Prolonged bed rest (Wood, 1956) and anticoagulants (Wessler *et al*, 1956 ; Wood, 1956 ; Davison *et al*, 1956) have been considered to be of great value. Drugs like cortisone, aminophylline or priscoline may be tried but are of no value.

Illustrative Case

Case 2 (Final diagnosis : Heart failure secondary to repeated pulmonary embolism)—A fifty year old female was admitted to the hospital complaining of fever and breathlessness, cough with slight expectoration and oedema of the feet. Since the age of 48 years, she had been getting attacks of winter cough lasting for a few days only. Four months prior to admission she started getting intermittent fever with rigor associated with dyspnoea which was exertional to begin with but later became continuous. A month prior to admission, she developed cough with expectoration and was brought to the hospital in a semi-conscious state.

Physical examination at the time of admission revealed that she was dyspnoeic and cyanosed. There was oedema of the feet and body and the liver was palpable and tender. Pulse was feeble. B.P. was 90/50 mm. Hg.

C.V.S. revealed accentuated pulmonary second sound. E.C.G. showed right axis deviation and strain. Examination of the respiratory system revealed crepitation in both the lungs, more marked in the interscapular region. Spleen was not palpable. Laboratory investigations revealed haemoglobin to be 8 g. per cent with moderate leucocytosis. Inspite of oxygen inhalations, antibiotics and nor-adrenaline drip, her condition deteriorated and she ultimately expired. The clinical diagnosis of cor pulmonale was made.

Postmortem examination revealed that lungs were crepitant and several irregularly distributed small firm areas were present. No emphysematous bullae were seen. The microscopic examination revealed multiple pulmonary infarcts and organising thrombi in small- and medium-sized vessels.

The heart chambers and valves were normal with irregular intimal thickening of the main coronary arteries. Liver sections showed mild centrizonal congestion. Leg veins did not reveal any evidence of thrombosis. Pelvic veins could not be searched carefully for the primary site of origin of the emboli.

Comments—The exact cause of congestive heart failure in this case could not be ascertained clinically till the autopsy findings of multiple pulmonary infarcts suggested the possibility of repeated pulmonary embolism. As already indicated, sometimes it may be difficult to identify the underlying embolus, particularly if the clot is partially organised. The same difficulty was encountered in the present case where the microscopic examination of lung showed organising thrombi so that the underlying embolus could not be made out. Due to the fact that pulmonary infarction in the majority of cases is due to embolism and the antemortem clots in pulmonary arteries are usually the result of emboli (Belt, 1939; Virchow, 1956), repeated pulmonary embolism was considered as the cause of multiple infarctions found in this case, and the final diagnosis of repeated pulmonary embolism leading to pulmonary hypertension was made.

Summary

Rare causes of cor pulmonale like primary pulmonary hypertension and repeated pulmonary embolism are being gradually recognised. Both the diseases run a downhill course and their diagnosis can be made with certainty only on autopsy. Out of the fourteen autopsies that were performed in our hospital on cases of cor pulmonale during the last three years, two cases were due to these two rare conditions. Both the cases are reported. Pathogenesis of these two disorders has also been discussed briefly.

Acknowledgments

Thanks are due to Dr. B. B. Bhatia, Professor and Head of the Department of Medicine, for kindly allowing me to report the cases.

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A STUDY ON CORONARY VASCULAR SYSTEM

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The textbook description of coronary arteries and venous drainage of the heart is well known to students of medicine. But the real nature of distribution and anastomosis of the branches of coronary arteries cannot be studied by simply dissecting the heart. With a view to get a clear conception of coronary circulation, investigation has been in progress in different countries with the help of gelatine, barium sulphate and a suitable synthetic dye. A coloured solution of requisite consistency thus prepared is injected into the blood vessels, and the cast thus formed is not sufficiently strong to stand the digestion experiment. The investigation of coronary system by liquid latex (natural rubber latex) or neoprene latex (synthetic rubber, polymerised from isoprene or chloroprene) (Smith and Henry, 1945; Edwards and Edwards, 1959) or similar substances has been done in U.S.A., Italy and other countries. Still it is considered worthwhile to investigate on a wider basis for understanding the pathologico-anatomical relation of coronary circulation which may be of great interest to clinicians who have to deal with increasing incidence of coronary occlusion and similar diseases, as well as for the purpose of demonstration to postgraduate students.

Visualisation of coronary system has been made possible by injecting neoprene latex or liquid

latex into the coronary arteries. This makes a perfect cast of the blood vesesels and stands very well the corrosive action of the acid. Then by means of digestion experiments the distribution of coronary arteries can be demonstrated.

Materials and Methods

We started our investigation with liquid latex obtained locally and neoprene latex from du Pont & Co., and obtained fresh human heart from accident cases.

Preparations for injection of liquid latex or neoprene latex into coronary system :

For the purpose of investigation we followed Lieb's technique (1940) with certain modifications.

Fresh specimens of human heart were secured within 12 hours after death. The heart was then rinsed with tap water at room temperature until the chambers were free from blood and clots.

Two metal canulae with stopcock were inserted into the right and left coronary arteries through the coronary ostia in the aortic sinus. They were secured with a flap of endothelial tissue round the ostia by a bow-knot ligature. The coronary system was then irrigated with tap water at room temperature until the whole system was freed from blood clots and air.

The coloured solution was prepared with liquid latex or neoprene latex and a suitable dye supplied by I.C.I. The canulae were connected by rubber tubing with a pressure flask containing the coloured solution which was allowed to flow into the coronary system at a pressure of 120 to 140 mm. Hg. until the vessels became prominent, thus effecting its distribution into the minute branches and precapillary plexuses. The distribution into capillary vessels, i.e., by injecting into the venous trunk, was also rendered possible by applying higher pressure (140 to 180 mm. Hg.) with frequent tapping and massage of the heart.

Soon after the injection, the heart was kept in a 4 per cent formalin-acetic acid solution for about 48 hours. By this procedure the myocardial tissue became sufficiently hardened and the coloured solution got solidified.

Digestion and Mounting Procedures

Owing to basket-like arrangement of the entire coronary system, it was necessary to have a supporting framework to keep in position the delicate rubber cast thus formed. So the auricular and ventricular cavities were filled up with the liquid latex, but without the dye.

This was also hardened by formalin-acetic acid solution as before. The heart was then immersed in strong and pure hydrochloric acid and kept there for about 48 hours.

But before the heart was placed in the acid, a solid glass rod was inserted through the ventricular cavities just below the atrioventricular groove with the ends bent upwards so that the specimen could be handled easily.

The myocardial tissues were found completely digested by the acid in 48 hours.

After washing the specimen carefully with tap water to remove all digested tissues and the acid, the coronary system with all its minute branches, precapillary and capillary plexuses became beautifully visible and could be readily studied. In order to prevent the minute branches and capillaries from matting together the specimen was kept immersed in water.

Discussion

The size and shape of the finished specimen suspended in water were quite in conformity with those of the original heart. On close examination the principal coronary arteries and their branches, big and small, could be identified clearly. The branches derived from main arteries were found to pass obliquely downwards over the heart, especially in larger number on the left side.

At the lower end they broke up into minute branches uniting with one another and forming precapillary plexiform network almost simulating jejunal and ileal branches of superior mesenteric artery. Thus they formed intracoronary anastomosis maintaining almost the character of end-arteries (Figs. 1 and 2, *vide* plate).

In one specimen (Fig. 3, *vide* Plate) the venous capillaries were distinctly visible and were found to drain ultimately into the coronary sinus. They were superfical and distributed so thickly that not only the arterial distribution but also the cast of the ventricular cavities were kept out of view, especially on the diaphragmatic surface (Figs. 3 and 4, *vide* Plate).

In another specimen (Fig. 5, *vide* Plate), there were intercoronary anastomosis between the anterior interventricular branch of the left coronary artery with the inferior interventricular branch of right coronary by numerous straight and oblique branches traversing through the interventricular septum, which was digested by hydrochloric acid.

The left ventricle was found more richly supplied with blood vessels with intra- and intercoronary anastomosis than the right one.

A very well marked and important fact noticed by us was that the sternocostal surface of the right ventricle close to infundibulum, about $1\frac{1}{4}''$ in diameter, was the least vascular area (marked by arrow in Figs. 4, 2). It is mentioned in texthooks that an infundibular branch is

responsible for the blood supply of that area (Baroldi and Scomazzoni, 1956) but it is doubtful if that small branch which was distinctly visible in our specimens can supply adequately blood to such a big area. Probably it gets a further supply through intercoronary anastomosis. This point requires further investigation. We worked with several specimens but always got the same result.

The auricular chambers got a fair distribution of minute branches with inter- and intracoronary anastomosis, but they were thinly distributed.

Summary

The anatomical details of the vascular system of the heart are presented in this paper. The technique of making cast of blood vessels by natural rubber latex or neoprene latex followed by digestion process is a helpful and scientific approach for studying anatomically and histologically the vascular system of any organ, both normal and pathological.

Owing to the stabilising action of aqurex-D, the specimens prepared with neoprene can be kept for a longer time without any deterioration. Natural latex available locally forms a much better cast, but we must find out some stabiliser to stop early deterioration.

The branches of coronary arteries anastomosing only at the capillaries are well demonstrated, suggesting that they are of endarterial type.

Least vascularity in a wide area on the sterno-costal surface close to the infundibular area is another constant finding of great interest.

Acknowledgment

We are indebted to Dr. S. P. Neogy, Professor of Physiology, Calcutta National Medical Institute, for the suggestion that liquid latex or neoprene latex may be used for the investigation of coronary system.

Our grateful thanks are due to Dr. A. B. Mukherjee, Professor of Clinical Medicine, for his encouragement and suggestions and to Dr. K. N. Bagchi, our Principal, for his valuable help in solving many difficulties in the course of this investigation.

Neoprene latex was supplied by the Rubber Laboratories of E. I. du Pont De Neumerous & Co. Ltd., New York, U.S.A., for this investigation. We are grateful to them.

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PRACTITIONERS' SERIES

CIRRHOSIS OF THE LIVER

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Periportal or Laennec's cirrhosis is frequently met with in this country, because the known aetiological factors, inflammatory as well as nutritional, are present in this subcontinent. Hepatitis, especially of viral origin, is recognised as an important cause of cirrhosis, especially in cases of prolonged or relapsing course. The interval between an attack of acute hepatitis and the first signs of cirrhosis, as proved by serial liver biopsy, varies from a few months to several years. The specific role of malaria and amoebiasis is less clearly established ; they, probably, act indirectly by interfering with the nutritional balance or, especially, the latter by favouring absorption of intestinal toxins.

Cholangitis or cholangiolitis, with or without stone, causing bile stasis lead to biliary cirrhosis. The prevention and treatment of this condition belongs more to the realm of surgery, and rather early surgery at that.

The role of malnutrition, especially protein deficiency, in the causation of Laennec's cirrhosis has been established in rats. It is not generally recognised in man and indiscriminate feeding of high doses of protein, as recommended in recent years, may cause more harm than good by precipitating a breakdown of the detoxifying functions of the liver, leading to an accumulation of nitrogen metabolities and, finally, to hepatic coma. Even methionine, one of the lipotrophic factors, has been shown to be contraindicated in 'decompensated' cirrhosis, because it increases the potentially dangerous nitrogen load. But the untoward by-effects of unphysiologic amounts of protein in late stages of cirrhosis do not refute the importance of a sufficient amount of nutritional protein in the prevention of this disease, particularly if it is combined with a balanced vitamin supply. The role of alcohol, although fully established, is not clear in its mechanism. That it is not possible to produce cirrhosis in any animal by alcohol alone is no argument against the alcoholic origin of cirrhosis in man. While there is no doubt that many hard drinking consumers of country liquor in Rajasthan die of typical Laennec's cirrhosis, it is equally certain that in the same area some teetotaller brahmins and banyas or even women who never tasted a drop of alcohol are equally afflicted

and that, on the other hand, some heavy drinkers live to a ripe old age without developing any liver trouble. It has been claimed that alcohol acts only partly by its direct toxic effect, while greater liver damage is caused by alcohol gastritis which leads to malnutrition with protein and multiple vitamin deficiencies.

The clinical picture of cirrhosis depends on the stage of development. The earliest complaints are usually constipation, flatulence, heaviness and discomfort in the epigastrium. The liver becomes easily palpable with a firm and uneven surface and a blunt edge, without any tenderness on pressure. Of liver function tests, the Takata Ara reaction might have become weakly positive and electrophoretic examination shows an increased plasma gamma-globulin content ; liver biopsy permits the diagnosis, particularly if done under the guidance of the peritoneoscope, often even before any of the function tests becomes fully positive.

Most of the patients present themselves for examination only when portal hypertension has already developed, characterised by enlargement of the spleen and, later on, formation of ascites in addition to the considerably enlarged cirrhotic liver. At this time there appears a grayish-yellow discoloration of the face with a dirty tinge of the cornea, the development of palmar erythema, stellate or spider-shaped dilatations of precapillaries at the upper half of the trunk, or the mucous membranes of nose, mouth or lips and, more frequently still, loss of body hair, especially of chest and axillae, with a varying degree of gynaecomastia, which gives the impression of some feminisation.

Slowly the size of the liver decreases, the margin becomes sharp, whereas the spleen becomes easily palpable, unless hidden by ascites. The last stage, that of atrophic cirrhosis has been reached, and finally, the liver recedes upwards beyond the costal margin.

Not rarely these changes are welcomed by the patient and the doctor as signs of improvement, because the liver enlargement has disappeared, and the weight has increased. That the former is due to the loss of parenchyma and shrinking of the fibrous tissue, and the latter to ascites is too often forgotten.

At the same time the whole appearance of the patient changes in a characteristic way. The face, neck and the hairless trunk become emaciated, while the girth (width) steadily increases, resulting in a pear-like shape. Far advanced cirrhosis leads either to haemorrhages from the gastrointestinal tract, especially oesophageal varicosities or piles, or in deepening jaundice and ascites, ending in hepatic coma. The haemorrhages, that are the result of portal hypertension and vitamin K deficiency, might stop spontaneously or by balloon compression of the oesophageal veins or by one of the shunt operations which relieve the portal pressure by creating new communications between portal and systemic circulation. Nevertheless, they are extremely serious danger signals indicating organic changes in the periportal fields that are most probably irreversible. Therefore, where proper surgical skill and experience are available, one of the shunt operations should be seriously considered, as at such a late stage they give probably the best chance to secure an additional span of useful life. This is also the last chance and psychologically a very impressionable one, when there may still be some chance of benefit from stopping alcohol intake in any form.

The appearance of jaundice in cirrhosis is more ominous still, as it signifies a breakdown of essential liver functions and usually is followed after a fairly short time by hepatic coma.

Management

Treatment must take many aspects into consideration—established or even suspected aetiology and all the recommendations made in world literature, provided their sources are reliable. This is so because with the course of cirrhosis spread over many years and the difficulty, particularly in India, to follow up cases over long periods, it is not possible to rely on one's personal experience only, particularly as there is no one treatment which is effective in all cases, and there is no treatment that can cure an advanced case of cirrhosis. On the other hand, there are many means at our disposal to improve liver functions, or even the liver structure histologically and also to reduce or stop formation of ascites.

Treatment is started by regulating the diet. The first and foremost step is to stop alcohol forthwith—whisky, gin or country liquor are probably equally undesirable. As long as the cirrhosis is 'compensated', i.e., there are no signs of accumulation of nitrogen metabolite, such as loss of appetite, nausea or neuropsychiatric signs of threatening coma, a fairly normal diet with the usual proportion of protein : carbohydrate : fat is permissible. Restriction of proteins is not indicated at this stage. But as soon as irritability or other personality changes, disorientation, flapping tremors, drowsiness, etc., appear pointing to 'decompensation' of the metabolic liver functions, all nitrogen sources in food and drugs (methionine) should be cut out. At the first sign of ascites formation the sodium intake must be restricted to a minimum by replacing sodium chloride by potassium salts. Vitamins, especially

those of the B-complex group and lipotrophic factors should be given in plenty.

In cases with a history of fever not long ago or with a leucocytosis without a tender liver, tetracyclines should be given and whenever there is an acute deterioration in the course of illness, such broad-spectrum antibiotics should be tried.

If malaria or amoebiasis play some part in the past history, these conditions should be eradicated. In amoebiasis not only the intestinal foci but also possible localisations in the liver should be fully treated (emetine, chloroquine).

Once such preliminary operations have been finished, the most effective treatment at our disposal has to be started, viz., intravenous injection of liver hydrolysates which have no haemopoietic but have only a liver protecting or rehabilitating effect (Ripason, Proheparum, B_{12} with Folic acid). This treatment should not be started unless the patient agrees to a very long course. We start with 1 c.c. intramuscularly for 2 consecutive days to exclude allergic patients, and continue with 1 c.c. diluted with glucose solution intravenously increasing every day by 1 c.c. upto 4 c.c. This dose is repeated daily for at least 4, sometimes even 6 weeks ; and then injections of the same dose are given on alternate days for 4 weeks ; and finally, the same dose is repeated twice a week for one year, and once a week for an unlimited period—the longer, the better. The greatest difficulty is to secure the co-operation of the patient for a sufficient length of time. If the veins are not suitable, injections should be continued by the intraglutaeal route. If this treatment has been started in fairly good time, one may confidently expect improvement of appetite and physical and mental efficiency, diminishing of ascites and oedema, improved plasma protein picture, and finally, even histologic proof of increased regeneration and diminished fat infiltration and fibrosis. Improvement of general condition, diuresis and drying up of ascites can be speeded up by giving prednisone, prednisolone or dexamethasone along with liver hydrolysates, starting with 30-40 mg. of prednisone and prednisolone, and about 4 mg. of the latter and decreasing the dose very slowly. How long a maintenance dose should be given depends on individual conditions, not the least on financial circumstances. The diuretic effect, in cases with pronounced or quickly increasing ascites with or without oedema, can be enhanced by the judicious use of chloro- or dihydro-chlorothiazide. As these diuretics cause loss of potassium which might precipitate the development of coma, their use in liver cirrhosis must always be accompanied by regular intake of 2 to 3 g. of potassium chloride per day. The use of ammonium chloride is contraindicated in cirrhosis as it produces acidosis which might prove dangerous in failing liver function.

Other methods of treatment which have been recently recommended are testosterone, because of its anabolic effect ; and vitamin E which in animal experiments protects the liver against necrotising agents. Russian authors found beneficial effects with vitamin B_{12} in 1000μg doses, and of pyridoxine in doses of 2 to 3 g.

There is one word of caution regarding aspiration of ascites. The liver is very sensitive to changes in intra-abdominal pressure, and sudden reduction as caused by paracentesis often has deleterious consequences. Haemorrhages as well as hepatic coma have developed so soon after aspiration even of small amounts of ascitic fluid that a causal connection is hardly doubtful.

In threatening or manifest coma, the terminal stage of Laennec's cirrhosis, one starts an intravenous 5 per cent glucose drip infusion with added vitamin-B complex and C. Vitamins A and K should be given separately. Tetracyclines are often useful, probably by diminishing absorption of nitrogen metabolites from the bowels, the bacterial flora of which is radically changed by these antibiotics. Whether to inject them or give them orally depends on the condition of the patient. The cortisone preparations or ACTH often give some relief. But it should be understood that there is a fundamental difference between coma due to acute hepatitis and that in cirrhosis. In the former, cure can be achieved and a life saved, in the latter some reprieve, some delay in the inexorable course of an invariably fatal disease is the best we can hope for.

SPECIAL ARTICLE

THE ROLE OF ANTHROPOLOGY IN SOCIAL AND PREVENTIVE MEDICINE

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INTRODUCTION

The recent interest shown by physicians and public health workers in the psychological and social aspects of disease has resulted in the recognition of multi-causal aspects of illness. Public

health and social medicine differ with respect to their approaches and the historical background under which they developed. Public health arose out of the urgency to control epidemic and communicable diseases. Its main concern was sanitation and environment. That this is not enough have been proved in the Influenza pandemic of 1918-19. Social medicine developed from a more scholarly European tradition, which included the work of Virchow (also an anthropologist), Meyenne, von Pettenkofer, Grotjahn and Ryle which modified and widened the concept of environment with the concept of culture—the subject matter of cultural anthropology (Caudill, 1953).

As a total study of man, anthropology has contributed valuable techniques to several branches of medicine—especially to history of medicine, forensic medicine, social medicine, and the science of comparative anatomy. In an earlier communication (Hasan and Prasad, 1959), it was shown that an integrated knowledge of physical anthropology, prehistory and social anthropology may be useful in the study of medicine. It is proposed to discuss in this article the role of integrated anthropology (physical as well as cultural) in social and preventive medicine, so that medical students, public health workers, research workers and administrators may be better equipped to improve social and health services.

Peculiarities of Anthropological Discipline

Paul (1956) pointed out two peculiarities of the anthropological discipline in contrast to other social sciences. They are of interest to both—medical men and anthropologists—in biological approach (physical anthropology) and also sharing of interest in ecological approach. While other social scientists are interested in the social environment only, anthropologists are interested in the natural environment also. The three social sciences, viz., sociology, social psychology and anthropology differ in their approaches to the problem. Social psychology provides us with experimental data ; sociology leans heavily on the use of questionnaires and interviews, most commonly single interviews of many people ; while anthropologists depend on field notes, based on personal observations and, as a rule, on repeated and extensive interviews with a small number of people.

The difference between sociology and anthropology is reflected in the type of population which the workers, in their respective fields, deal with. Anthropologists prefer to choose small communities like the part of a tribe or a single village, because of the greater accuracy for first-hand observation. This is known as the microcosmic approach. Anthropology is also a comparative science. Thus by microcosmic technique the anthropologists not only try to get a general pattern but also the degree of variation from it, and also the reasons for such variation. This technique is often used for producing a macrocosmic theory. The microcosm is used to illuminate the macrocosm—the particular to illustrate the general. Another characteristic feature of anthropological inquiries is that they are holistic in approach. Anthropologists may select a particular item for examination, but they try to see it with regard to its place in the total *milieu*, and the life of the human group concerned (Firth, 1951).

Social Anthropology in Social and Preventive Medicine

Progressive medical workers believe that culturally determined habits such as the manner of easing, eating, sleeping and social customs such as exogamy, endogamy and polygamy play important role in the control or maintenance of disease. For example, the high incidence of venereal diseases among the *Khasas* of Jaunsar Bawar area of the Dehra Dun district in Uttar Pradesh is due to the practice of polyandry and in spite of Government efforts no progress has been made in their control. The chances of reinfection are great as there is one wife among several brothers and even when she is treated she is reinfected and in turn infects others. A change in social institution seems necessary for controling venereal diseases in such a community.

In India little effort has been made to collect data indicating social causes in health and disease. Majumdar's (1958) recent analysis of primitive medicine emphasises that a study of medicine of a society (folk medicine) and the methods of healing are no less important for a complete understanding of the total way of life of a people than its social institutions.

Many facets of primitive and folk medicine have a scientific basis and modern medical science has some of its origins in them (Fejos, 1959). Although the disease concept in primitive societies was magical in anthropological sense, mny important and efficacious drugs such as quinine, ephedrine, etc., and recently the rauwolfia alkaloid from India have been assimilated into western medicine. Thus studies of folk and tribal medicine should be undertaken in India by anthropologists and workers in social medicine. A study of kwashiorkor in Africa has revealed that this advanced protein malnutrition in children is con-

nected with their defective feeding habits. The use of animal milk is unknown among some African tribes. A study of the customs followed in different areas in the weaning of children and in feeding children between weaning and puberty is necessary. "These should be studied by competent social anthropologists with some knowledge of nutrition" (Brock and Autret, 1952). The prevalence of kwashiorkor is less in India, as milk is recognised as an important item of diet for health and usually given to growing children, and sick, and weak persons. This proves that health and disease are associated in some way with beliefs, attitudes, values and customs.

Prevention of disease is dependent upon our ability to improve the social or environmental factors. Thus by studying the customs, values, attitudes and beliefs of the people in different cultural areas and cultural levels, the health administration may find it convenient to frame social policies and it is easier to bring about improvement. This was realised by the Conference on environmental sanitation which was held in 1956 at New Delhi. A number of anthropologists pointed out that although the people are indifferent to their health and wealth, signs of change and new values of cleanliness and orderliness are now evident in the village life. The most important problem in Indian villages is the safe disposal of human and animal wastes. Progress in environmental sanitation is impossible without health education. Paul (1955) advocates that before asking a group of people to assume new health habits, it is wise to ascertain their existing habits, how these habits are linked to one another, what functions they perform, and what they mean to those who practise them. The concept of culture as one of the environments should be recognised. Culture, the subject matter of cultural anthropology, has been defined as the total way of life. Anthropologists, therefore, study the effects of conditions in which men are born, live, work, enjoy themselves, procreate and die.

An example of how understanding of the total way of life of a people may equip the public health workers with an awareness of socially regulated customs and practices is the study of food habits and food taboos. The orthodox class in India can hardly be persuaded to eat meat. Even those who take meat have objection to eating certain types of meat like beef or pork. Certain castes among Hindus, whose diet consists of excessive carbohydrates and fats but is poor in proteins, are prone to certain types of diseases (Gangulee, 1939). Over-eating of carbohydrates and fats, the chief dietetic error of the well-to-do Hindus, produces metabolic disorders. The predominance of cereal foods, the preference for vegetables and fruits, the fondness for milk and milk products, and the consumption of sweets are the main features of an orthodox Hindu dietary ; and these have not substantially altered with the march of time.

The majority of people in India are conservative in regard to the choice of food. They do not easily take to any change in their food habits. The increasing consumption of wheat among the rice eating people (and *vice-versa*), the use of refined sugar in place of jaggery, the use of vegetable oil in place of *ghee* (cooked butter), the use of skimmed milk powder, and of tinned foods like condensed milk, tinned fruits and vegetables are some of the instances which tend to show that conservatism in India may not offer a serious obstacle to bring about innovations in their dietary, especially among the urban and suburban areas. Higher education, contact with other communities, rise in the standard of living and availability are helping us in this direction.

A few examples, of how important it is to understand the total way of life of a people before introducing a change in the habits of the people, and before health planning, may be given here. The value of the intake of unrefined food prepared indigenously needs to be recognised against the background of the cultural and biological needs of the people. Replacement of par-boiled or hand-pounded rice by milled rice in the diet can lead to vitamin-B deficiency. Use of sugar in place of *gur* (jaggery) may remove a rich source of iron in the diet with the result that the rural people who are often infested with ankylostomiasis may suffer from anaemia.

Paul (1955) advocates the inclusion of case-study approach of anthropology in public health teaching. He mentions three contributions that the case-study approach of anthropology can make. These are (a) conveying social science concepts in a palatable manner ; (b) gaining respect for cultural difference ; and (c) teaching that culture is more than a collection of customs or that culture is not a mere collection of items but tends to be a system.

Social Anthropology and Paediatrics

Social anthropology has concerned itself with the study of the particular forms of social interaction between persons and the derivatives of those interactions in particular cultures. It has thus influenced considerably the field of paediatrics. Spence (1955) is of the opinion that in addition to hospital, which is an institution for the treatment of disease, the chief instrument for child welfare in modern society is, or should be the mother and the chief instrument for the childs' development

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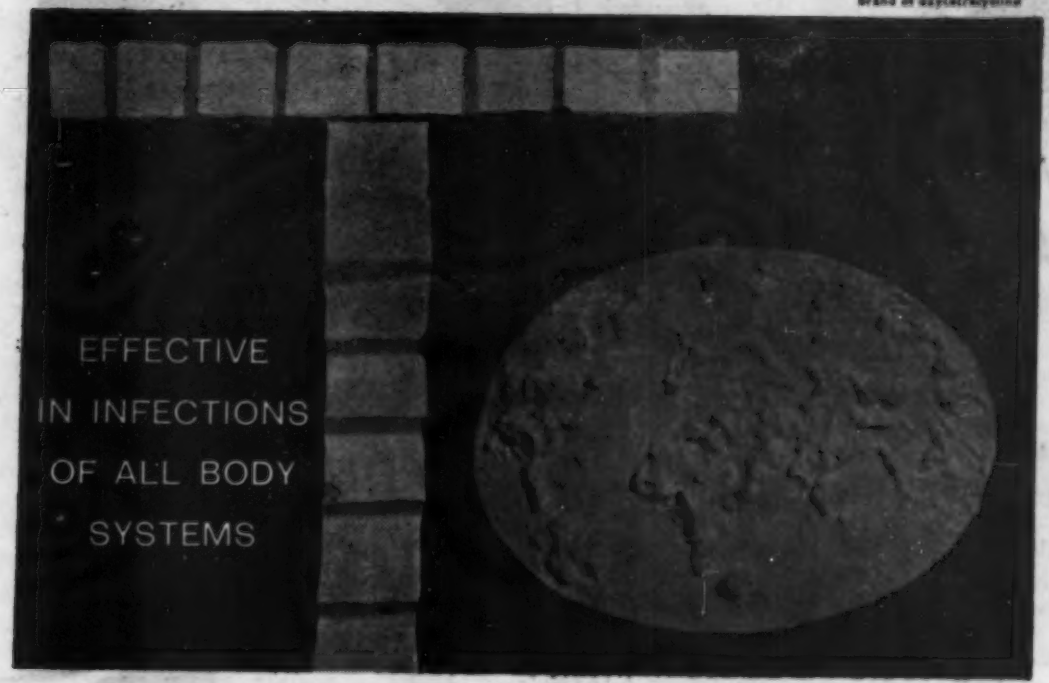

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should be the family. Paediatrics should now turn itself to an objective study of these factors. Considerable light has been thrown by anthropologists through a comparative study of child-rearing disciplines in different cultures, from which it has been inferred that all human beings require the same kind of satisfaction of their basic needs. The anthropologists have unravelled the roles of carrying, feeding, cradling, etc., in moulding and developing the personality. The pioneer investigations of Mead (1928, 1930, 1935) have drawn attention to such factors.

Social Anthropology in Psychosomatic Medicine

The demonstration that feelings and somatic functions are interrelated, has resulted in the development of psychosomatic medicine. Numerous anthropological studies of primitive people have demonstrated the importance of cultural factors in the psychosomatic as well as psychological development of the person (Montagu, 1957). A man may find that he has broken a *taboo*, the punishment for which is inevitable death. Up to this moment he was in quite normal health, but from then on he wastes away and in a short time dies. Ackerknecht (1944) has demonstrated the role of 'way of life' (or culture) in his study of psychological and physical peculiarities of white children abducted and reared by North American Indians, and shown that children who grew up among these people became Indians mentally and to a certain extent even physically.

The concept of culture as an environment offers a much deeper and more effective understanding of psychosomatic diseases and their treatment. The psychosomatic investigator is concerned with the individual, the anthropologist is interested in the group, which consists of individuals and it is at this nexus that psychiatrist and anthropologist can be of the greatest help to one another (Montagu, *loc. cit.*).

Northrop (1959) pointing out the relationship between cultural mentalities and medicine recognises the contributions of anthropological researches in developing such an insight. He has framed certain principles. These are (1) Medical science to be effective must pay as much attention to cultural mentality of the patient, as to the chemistry of the disease; (2) Medical science is more than a set of concrete practical prescriptions for the cure of specific unhealthy conditions. A comprehensive way of thinking about every fact of nature and every act of daily life is a part of the physician, public health worker and the patient; and (3) The effectiveness of a drug in controlling the bacterial infection depends not merely on the demonstrated chemical capacity of the drug to kill that bacterium *in vitro* but also on the waking, sleeping, and other habits of the people to whom the drug is given.

The phenomenon of cultural transmission and change due to first-hand contact is known as acculturation, and the study of acculturation throws valuable light upon the physiology, as it were of culture and cultural changes. Leighton (1959) maintains that acculturation, when rapid and extensive, has a damaging effect on mental health of the people. The study of the role of acculturation on mental health is within the general framework of social and preventive medicine and constitutes a meeting place of one branch of medicine (psychiatry) and one of the social sciences (anthropology). Its value lies in the hope it offers of devising methods for reducing and preventing mental illness. The rapid urbanisation either due to industrialisation (Jamshedpur, Rourkela towns), or due to other developmental activities (the development of a town by the side of Rihand Dam in the Mirzapur district, U.P.) offers good opportunities for Indian psychiatrists and anthropologists to test the hypothesis put forward by Leighton.

Physical Anthropology in Social and Preventive Medicine

The recognition of the interdependence of health and social forces has dismissed the viewpoint that biology and sociology should deal separately with two aspects of man—biological and social, and has strengthened the view of those who believe in a combined sociocultural and biological approach. The problem of race is an excellent example which anthropologists have studied with this viewpoint. In the same way, the effects of different socio-economic and physiographic environments and of illness upon growth have been studied by physical anthropologists. Their findings almost invariably show significant relationships between all these variables. One of the earlier and pioneer studies in this field is that of Boas (1940). He demonstratd changes in the head form in children of immigrants from Europe born in U.S.A. as compared to their parents who were born in a variety of localities in Europe.

Anthropological studies of growth and development of children have shown that there are two important factors which affect them, heredity and environment—nature and nurture. This work has influenced medicine as a whole in general, and social medicine in particular. Nutritional assessment of school children by somatometric data and somatometric indices has been done in

India (Prasad, 1949). It is pleasing to note that the Indian Council of Medical Research are now taking keen interest in the study of growth in Indian infants and children and have started a number of studies in various parts of the country with which anthropologists are closly associated.

Another important contribution of physical anthropology to preventive medicine lies in the control, cure and prevention of hereditary diseases. The preventive method is employed by searching among the blood relatives of a patient, suffering from a hereditary disease, an early preclinical and laboratory sign of the disease. When these are found, appropriate preventive measures may be taken (Hasan and Prasad, *loc.cit.*).

Conclusion

The need today in India is to impress upon students of medicine that diseases must be seen in their multicausal aspects and against the background of the cultural level of patients. This has been demonstrated clearly by Prasad *et al* (1960) in their study of tuberculous families in Lucknow city. The study of patients in their family has become important for the medical students for understanding man in disease, rather than disease in man (Prasad, 1960).

Summary

1. The role of integrated anthropology (physical and cultural) in social and preventive medicine has been discussed in this paper.

2. The three social sciences, viz. sociology, social psychology and anthropology differ with respect to their approaches and focus of interest. The biological-ecological approach is common between anthropology and medicine.

3. Prevention, the main aim of preventive medicine, is dependant upon the ability to improve social and environmental factors. This demands a thorough undersanding of the way of life (culture) of a people. Social anthropology can help medical students, public health workers, research workers and administrators in this respect.

4. Paediatrics should now turn itself to an objective study of child-rearing practices. The collaboration between anthropology and paediatrics can prove to be fruitful in this field.

5. The concept of culture as an environment offers a much deeper and more effective understanding of psychosomatic diseases and their treatment.

6. There are two important contributions of physical anthropology to social and preventive medicine (a) in the study of the role of socio-economic and physiographic environments upon growth and health ; and (b) in the control, prevention and cure of hereditary diseases.

7. The need today in India is to impress upon students of medicine that diseases must be seen in their multicausal aspects and against the background of the cultural level of patients.

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CASE NOTES

NEUROLOGICAL MANIFESTATIONS OF SARCOIDOSIS

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INTRODUCTION

Sarcoidosis is a disease of unknown aetiology and the number of cases reported in this country is very small. It is a granulomatous lesion which affects mainly the skin, lymph nodes, lungs, eyes, liver and spleen and in fact it may affect any tissue. Histologically, the lesion is characterised by formation of nodules of epithelioid cells without central caseation and with little or no inflammatory mass. Multinucleated giant cells may also be present. The diagnosis of this disorder with diffuse systemic affection is not difficult when it is associated with classical sarcoid manifestations like lymphadenopathy, skin lesions, iridocyclitis, enlarged hilar lymph nodes, and can be confirmed by histological examination of the biopsied material. Neurological dysfunctions have also been noted in sarcoidosis; and sometimes these may be the protean manifestation of the disease. The purpose of this paper is to report one histologically proven case of sarcoidosis presenting with recurrent multiple cranial nerve palsies and paroxysmal hypertension, and to review the literature on the subject.

NEUROLOGICAL MANIFESTATIONS :

In 1909, Heerfordt described uveoparotid fever as a type of sarcoidosis characterised by swelling of salivary glands, inflammation of the uveal tract and cranial nerve involvement. Later on, many cases of sarcoid polyneuropathy were described with uveoparotid variety of sarcoidosis. Lately, authentic cases have been reported describing the central nervous system, spinal cord and meningeal involvement in sarcoidosis.

The nervous dysfunctions in sarcoidosis may be present either alone or in association with signs of other tissue involvement. These may manifest in four ways : (1) cranial or peripheral neuropathy, (2) C.N.S. involvement, (3) meningeal affection and (4) mixed form.

1. *Cranial and peripheral neuropathy*—Neuropathy is the commonest mode of presentation of sarcoidosis having noteworthy features :

(a) Cranial nerve palsies which are more common, may occur either alone or in combination with peripheral neuropathy, and may be unilateral or bilateral. Either of them (cranial and peripheral neuropathy) may present with multiple nerve lesions.

(b) The paralysis is transient and recovery, complete or partial, in a few weeks to a few months' time, is the rule. Relapses are known to occur and may affect the same side or the other.

Almost all the cranial nerves have been reported to be involved in sarcoidosis. A brief summary of these manifestations of cranial and peripheral nerve involvement, is given below :

Cranial neuropathy :

(i) Facial nerve palsy : commonest. It may occur as part of uveoparotitis or may simulate Bell's palsy.

(ii) Optic neuritis or papillitis.

(iii) External ocular palsies and ptosis.

(iv) Trigeminal sensory loss and loss of taste.

(v) Nerve deafness.

Peripheral neuropathy :

(i) Pain : a common feature.

(ii) Sensory loss simulating acute infective polyneuritis or mononeuritis multiplex.

(iii) Lost or absent tendon reflexes.

2. *C.N.S. involvement*—Signs of central nervous dysfunction are very rare manifestations and can affect cerebral hemisphere, basal ganglion, hypothalamus, pituitary, cerebellum, brain stem and spinal cord.

Unlike neuropathies, signs of central nervous dysfunction tend to progress or remain stationary over a long period. Regression is rare.

3. *Meningeal involvement*—This is also a rare presentation of sarcoidosis and may manifest as frank meningitis of subacute or chronic onset, or as latent one which can be suspected on C.S.F. examination.

4. *Mixed forms*—In this variety, signs of central nervous system involvement, meningeal affection and neuropathies are present either simultaneously or separately in the course of illness.

The diffuse nature of involvement is liable to cause error in diagnosis particularly in atypical cases unless associated with generalised systemic manifestation. The following is the report of one such patient where the case remained a puzzle to us until the histological study of a lymph gland enabled us to make the correct diagnosis.

CASE REPORT

Shanti, female, aged 32, was admitted to the hospital on 14-9-1959 with the following history : At the age of twenty-nine, she had an attack of sudden paralysis of the right facial nerve along with pain in the right ear, which lasted for two months, and she recovered gradually. Two years later, she again had facial paralysis, but this time on the left side, along with severe pain in the left ear which lasted for 15 days. She again recovered completely. A month later she got pain in the right hemicranium with anaesthesia and numbness of the right side of the face lasting for 6 months, during which period she had severe pain in the right eye with sudden diminution of vision in the same eye. She was admitted into a hospital for this trouble.

Clinically she had hypertension (190/120 mm.

Hg.) with no renal or cardiac involvement. No facial palsy was noted. X-ray of the sinuses revealed poorly developed frontal sinuses; but ethmoidal, maxillary and sphenoidal sinuses were clear. Funduscopy of the right eye revealed optic neuritis with central retinitis. W. R. and V.D.R.L. tests were negative. She was discharged undiagnosed. Subsequent check-up showed normal B.P. record and normal fundus picture.

Second admission—The patient remained well until three months prior to the present admission when she started getting dull aching pain in the left hemicranium and back of the neck, with occasional exacerbation. She also started getting tingling and burning sensation in the left upper extremity and the left side of the face, and a sense of formication of the left lower extremity, and attacks of dyspnoea. One month prior to admission, she suffered from diplopia in the left eye and inability to move the left eye outwards, and so she was admitted in the wards.

Physical examination—The patient was of average build. Her blood pressure on admission was 130/90 mm. Hg. Subsequent B.P. records showed paroxysmal attacks of high blood pressure during period of hospitalisation ranging from 180/110 to 180/120; each attack lasting for a few hours only. A few almond-sized lymph glands were palpable in the right axilla. Her abdomen, and the respiratory and the cardiovascular systems were normal. Neurological examination revealed paralysis of the left rectus and nerve deafness in the left ear. No facial palsy was detected. Fundi of both eyes were normal. Plantar reflex was flexor on both sides.

C.S.F. examination revealed normal tension with sugar 60 mg. per cent, proteins 40 mg. per cent, and chlorides 670 mg. per cent, with less than 5 cells per c.mm. The W.R. and V.D.R.L. tests were negative. The E.S.R. was 16 mm. (Wintrobe). Total serum proteins were 8·4 g. per cent; serum albumin 3·7 g. per cent. Serum calcium was 10·8 mg. per cent. X-rays of the skull, hands and lungs were normal. Tuberculin test was negative.

A lymph gland from the right axilla was biopsied. The lymphoid follicles showed a large number of tubercles consisting of lymphocytes, epithelioid cells, and Langhan's giant cells. No caseation was seen in these tubercles. There was increase in collagenous fibres round about and inside the tubercles.

With the report of histological examination (Fig. 1, *vide* Plate), the diagnosis of sarcoidosis was confirmed.

Follow up—The patient was kept on cortisone therapy. Two weeks after commencement of the therapy, the patient could move her left eye outwards and her diplopia disappeared. Physical examination on 14-1-1960 revealed that her B.P. was 135/75 mm. Hg. There was no residual sixth nerve palsy. Nerve deafness in the left ear was very minimal. The patient still complained of occasional tingling sensation on the left side of the face and tinnitus in the left ear. Past B.P. records revealed that only once (18-11-59) she had hypertension (180/120 mm. Hg).

Discussion

This patient presented transient but recurrent attacks of cranial and peripheral neuropathies. The various manifestations suggested the involvement of the second, fifth, sixth, seventh and eighth cranial nerves at one time or the other, along with paraesthesias in the distribution of the peripheral nerves. Besides these neuropathies, the patient had paroxysmal attacks of hypertension and dyspnoea. All these associated findings were suggestive of disseminated systemic involvement and were not explainable by one diagnosis. Transient neuropathies, particularly bilateral facial nerve palsy with complete recovery, suggested the possibility of sarcoidosis and the case was therefore investigated for it. A lymph gland from the right axilla was biopsied, and the histological picture confirmed the diagnosis of sarcoidosis.

Although, the nervous manifestations in this patient were quite suggestive of sarcoidosis, the attacks of paroxysmal hypertension were quite unique because such a finding had not been reported in the past in association with this disease. Considering the diffuse nature of sarcoidosis, one feels inclined to consider sarcoidosis as cause of paroxysmal hypertension, the mechanism of which may be difficult to understand in the present state of our knowledge.

Finally, it may be emphasised that pure neurological presentation of sarcoidosis is usually a diagnostic problem. The review of cases shows that one should strongly consider sarcoidosis in bizzare neurologic presentations particularly where transient cranial and peripheral neuropathies are a feature. Out of all, transient, bilateral facial palsy has been found to be the commonest presentation of sarcoid lesion.

Summary

The neurological manifestations of sarcoidosis have been reviewed along with a case report. The case was interesting firstly, due to its presentation primarily as a neurologic case; secondly, due to transient nature of cranial and peripheral neuropathies, a feature suggestive of sarcoidosis; and thirdly, due to association of paroxysmal hypertension with the disease. The diagnostic difficulty particularly in a purely neurological presentation without any other evidence of sarcoidosis, has been emphasised.

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Fig. 1—Diaphragmatic surface of the heart showing intracoronary anastomosis.

Fig. 2—Sternocostal surface of the heart showing intracoronary anastomosis.

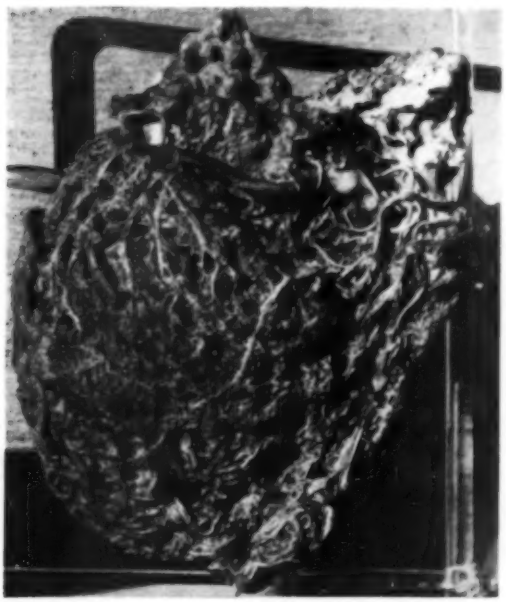

Fig. 3—Diaphragmatic surface of the heart showing coronary sinus with thickly set venous capillaries.

Fig. 4—Sternocostal surface of the heart showing the least vascular area in the infundibular region (marked with arrow).

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Fig. 5—Interior of sternocostal surface of the heart showing intercoronary anastomosis.

CHATTERJEE AND ROY—*A Study on Coronary Vascular System (p. 18)*

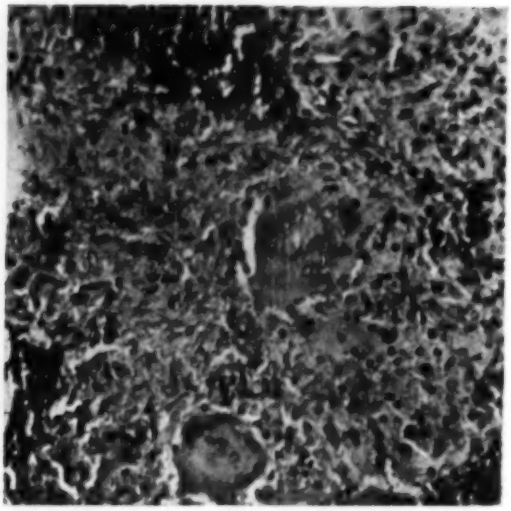

Fig. 1—Showing lymph gland exhibiting focal collection of epithelioid cells, and enclosing in their midst a few giant cells. There is no necrosis.

GUPTA and KATIYAR—*Neurological Manifestations of Sarcoidosis (p. 27)*

Fig. 1—Cut surface of the potato-shaped tumour showing variegated appearance due to haemorrhagic, necrotic and lipoid-laden areas.

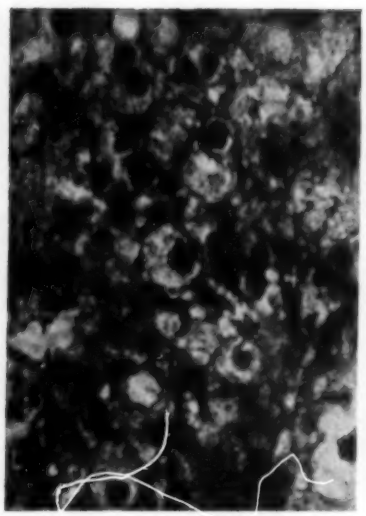

Fig. 2—Photomicrograph showing the characteristic large cells with faintly staining granular cytoplasm (H. & E. × 1400).

Fig. 3—Photomicrograph showing a lobule of tumour tissue surrounded by stromal connective tissue (H. & E. × 630).

RANGAM AND GUPTA—*Carotid Body Tumour (p. 31)*

CAROTID BODY TUMOUR

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Carotid body tumour was first described by Marchand in 1891. Since then over 300 cases have been recorded (Byrne, 1958) besides a few from this country (Khanolkar, 1930; Krishnaswamy and Rao, 1941; Bhende, 1946; Sundarasivarao and Sampath, 1951).

The rather unusual situation of the tumour, the ease in its removal at operation and the total lack of clinical symptoms prompt us to report this case.

Case Report

A male, aged 34, was admitted into the hospital on 24-3-1959 for a gradually increasing, painless swelling in the right side of the neck, since 1 year. Clinical examination revealed that the swelling, measuring $4'' \times 2''$, was cystic and situated deep to the sternomastoid. There was no tenderness, pulsation or bruit. The swelling did not move with deglutition but could be moved laterally. Systemic examination and routine investigations revealed no abnormalities. The diagnosis at this stage was 'a degenerating malignant growth'.

An aspiration biopsy, performed on 2-4-1959, was reported as consisting principally of red cells, fibrin and leucocytes. A few slightly elongated cells interspersed amongst collections of lymphocytes were also seen. No definite opinion could be expressed on the nature of the swelling but there was no evidence of malignancy. The patient left the hospital at this stage.

The patient was readmitted on 2-6-1959 and was operated upon on 9-6-1959. The swelling underneath the sternomastoid was cystic, encapsulated and easily separable from the surrounding structures. It was not connected with the carotid vessels. In fact, a carotid body tumour was not considered any time at operation. The specimen was sent for histopathological examination with alternative diagnosis of bronchial or thyroid cyst.

Gross appearance (Fig. 1, *vide* Plate)—The swelling was roughly potato-shaped, faintly lobulated and measured $3'' \times 1\frac{1}{2}'' \times 1\frac{1}{2}''$. It felt cystic in some parts. The cut surface showed a distinct capsule all round from which fibrous trabeculae could be seen passing into the substance of the tumour, which consisted of solid yellowish areas intermingled with several cystic spaces containing haemorrhagic material.

Histopathological features—The tumour had a thick capsule of several strands of fibrous tissue and was highly vascular so that some parts looked haemangiomatous. Necrotic and necrobiotic changes were recognisable. The stroma of the tumour, formed by delicate strands of fibrous tissue was more prominent than the cellular component. The latter consisted of polyhedral cells with faintly staining granular cytoplasm and pale vesicular nuclei (Fig. 2, *vide* Plate). These were distributed either as linear columns between the fibrous strands of stroma or as numerous lobules surrounded by stromal connective tissue (Fig. 3, *vide* Plate). A blood vessel could be seen in many of these lobules, and immediately surrounding the blood vessel was a mantle of cells which looked quite different from the cells described above in that they were smaller, spherical and both their cytoplasm and the nuclei stained more compactly.

The diagnosis was 'carotid body tumour'.

Comments

Carotid body tumours would normally be expected at the bifurcation of the common carotid artery, but some tumours have no immediate anatomical relationship to the carotid artery or its bifurcation. There are instances where the operating surgeon did not consider a carotid body tumour as a possibility. In this case, the condition was not thought of but other possibilities (branchial/thyroid cyst) were suggested.

The carotid body itself is described as being situated on the postero-medial side of the common carotid artery, but similar tissue is known to exist in distant sites such as the superior bulb of the internal jugular vein, the mediastinum and the base of the neck (Hollinshead, 1958). An explanation for the unusual situation of some of the carotid body tumours could be sought in the disposition of the carotid-body-like tissue.

From the surgical point of view, in a few cases the tumour can be easily shelled out but in others adhesions to the carotid artery, jugular vein and large nerves, render it necessary to sacrifice parts of these structures. In the present instance, obviously due to its anatomical situation, it could be easily shelled out.

Acknowledgment

Our thanks are due to Dr. B. B. Ohri, Professor of Surgery, M. G. M. Medical College, Indore, for clinical details of the case and the specimen.

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JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION

CALCUTTA, JULY 1, 1960

THE PROBLEM OF MEDICAL EDUCATION IN OUR COUNTRY

Medical educationists all over the world are trying to evolve a better system of medical education. Before we attempt to think seriously in this direction, we must be very clear in our minds what is it that we are really to achieve.

The problems which confront the economically well advanced countries of the West are not exactly the same that face us. There could however be no two opinions that our primary aim should be to produce a good basic doctor. He should have a good grasp of the common diseased conditions prevailing in our country, learn to recognise them clinically and deal with their preventive, social and therapeutic aspects efficiently. Our curriculum then should be so worked out that a student is not burdened with unnecessary details. Cramming should be discouraged ; he should be taught to develop a scientific approach to his problems and should be trained to think and act for himself.

It is important that the future doctor should have a broadbased education in science and the humanities. This would not only enable him to grasp the subject matter taught to him but also to fit himself in the social structure in which he would have to work after qualifying. Unless the Higher Secondary school standard is brought up at least to the old Intermediate standard, the abolition of the Intermediate examination and institution of Higher Secondary school examination and subsequent pre-medical training and examination would not be an improvement on the previous arrangement and indeed may cause a further deterioration in the standard of pre-medical education. Further, though our need for qualified medical men is very great yet it is essential that proper selection of candidates should be made during admission to the medical colleges. Care should be taken to find out that the student has a minimum set standard of intelligence and education before he is considered for admission in a medical college.

The recent reduction of the course of medical studies to four years and a half has been a welcome move. Pre-clinical training in the basic sciences can be easily limited to one year and a half provided unnecessary details are cut out and too many holidays are not observed during the working sessions. During the period of clinical training more attention should be paid to practical training and to the day-to-day work of the students. A substantial percentage of marks should be allotted to the day-to-day working which should be considered when the final evaluation is done in the university examination.

The institution of internship has been a real forward step. The training should however be carefully planned and the students should also have opportunities during the period to familiarise themselves with the conditions prevailing in our villages.

While the need for a good basic doctor is of prime importance it is no less essential to have adequate facilities for specialist training in the different branches of medical science in our medical colleges and research institutions. Unless due emphasis is placed on this aspect of medical training, we shall be sadly lagging behind other countries in the field of the advancement of medical science and incidentally would also fail to produce the good basic doctor because both these aspects of medical education are so closely interrelated that one cannot develop adequately without the other.

Intimately connected with the problem of efficient undergraduate and postgraduate teaching is the question of proper emoluments to the teaching staff. While the move to have some wholetime teaching staff is welcome, it should be realised that all staff be properly paid. The scales of pay existing in some of the States are distinctly low. Even the scales recommended by the Medical Education Conference in New Delhi in March 1958 are not adequate. The argument often cited that candidates are still available on the present low pay scales is not a sound one. Are we really attracting the best talents available in our country? The answer is obviously in the negative. This has a serious and far-reaching effect. Already many good students are going in for engineering and other courses, if not for anything else, for purely financial reasons. The previous suggestion of having an All-India Medical Educational Service (whose members would man the teaching and research institutions) with an attractive and suitably graded pay scale and efficiency bars might, if implemented, probably attract suitable talents and would partly solve the problem.

I.M.A. PRESIDENT'S TOUR OF MAHARASHTRA

Dr. H. N. Shivapuri, President of the Indian Medical Association left Lucknow on the morning of April 22nd and reached Jalgaon early next morning. He was received by Dr. B.B. Kirtane, President, Maharashtra Territorial Branch, I.M.A., and office-bearers of Jalgaon Branch. After breakfast he left by car for Aurangabad. On the way he was shown the Ajanta Caves and rather late in the evening reached Aurangabad where he was a guest of Dr. G. M. Shroff—Secretary of Aurangabad Branch. Next morning the President was taken round the Ellora Caves and Daulatabad fort, etc. In the eveing he addressed a meeting of the Branch at the Railway Hotel, Aurangabad. Among other things, he spoke about the Central Building Fund. The members of the Branch present promised to contribute their share of the fund. Dr. Shivapuri hopes they will collect and send the amount soon.

On 25th morning he returned to Jalgaon and a dinner meeting was held that evening by the Jalgaon branch at the residence of Dr. Devalbhakat. In Jalgaon he was also shown the Radhabhai sanatorium constructed by Dr. Bendale in memory of his mother. It is a cottage sanatorium for tuberculosis patients run by Dr. Bendale on very modern lines. In the meeting that evening in response to his address to the members, contributions amounting to about Rs. 1,900/- were promised. The biggest contribution was to the tune of Rs. 1,000/- by Dr. Bendale payable in four equal instalments.

Dr. H. N. Shivapuri, President of the Indian Medical Association, during a Visit to the Family Planning Centre of the Red Cross at Dhulia.

L—R—Dr. Shivapuri, Dr. Kirtane, Dr. Mrs. Chavan and Dr. Joshi, Joint Secretary of the Dhulia Red Cross.

Dr. H. N. Shivapuri Distributing Clothes to Needy Children at the Red Cross Building, Dhulia.

L—R—Rao Sahib Ransing, Secretary, Dhulia Red Cross, Dr. Shivapuri, Dr. Kirtane, Dr. Joshi and Dr. Karve.

On 26th morning Dr. Shivapuri left early in the morning with Dr. Kirtane for Dhulia where a programme had been arranged. In the morning a Red Cross show had been arranged where sweets and clothes were distributed to the poor children. In the evening he laid the foundation stone of the building of Dhulia Branch. Later he addressed a meeting of the citizens of Dhulia explaining to them what work the Indian Medical Association was doing for the public. At dinner time there was a meeting of Dhulia Branch of the Indian Medical Association where the contributions promised by the members of the Branch for the Central Building Fund of the Indian Medical Association amounted to about Rs. 1000/-. Dr. Shivapuri was the guest of Dr. Shah, Secretary of the Dhulia Branch.

On 27th morning he left early with Dr. Kirtane by car for Malegaon where they had breakfast with members of Malegaon Branch. Each member

present promised contribution for the Central Building Fund of the Indian Medical Association. After breakfast and the meeting, they left for Nasik reaching there before lunch. A meeting was arranged with the members of the Nasik Branch over lunch. Dr. S. C. Sen of Delhi and Major R. N. Bose of Meerut who were spending a holiday at Devlali (near Nasik) were also present at the meeting by special request. Addressed both by Dr. Shivapuri and Dr. Sen, the members of the Nasik Branch promised to contribute their mite to the Central Building Fund.

Dr. Shivapuri left by train and reached Kalyan in the evening. He addressed a meeting of the Kalyan Branch over dinner. Members of the Kalyan Branch promised to complete their share of an average of Rs. 50/- per member at an early date and send the amount to the Central Fund. From Kalyan Dr. Shivapuri went to Pllan where he arrived on 28th morning. A meeting of the Poona Branch was addressed by him on April 30th. The office-bearers of the Poona Branch promised to do their best for collecting money for the Building Fund of the Indian Medical Association.

In the opinion of the President the Branches in Maharashtra were fairly active, taking keen interest in all health and preventive measures. Nasik Branch had even a scheme for giving triple antigen to school children. He was greatly helped in the tour by Dr. Kirtane, President, Maharashtra Territorial Branch and by his co-workers. Dr. Kirtane was to send a detailed list of individual contributors to the Building Fund from the various Branches in Maharashtra. In all 7 branches were visited by the President.

On 5th of May the President visited the Allahabad Branch. Dr. S. C. Sen had visited this Branch about 2 years ago but no money had so far been collected for the Building Fund. In his address at the meeting of the Branch in the evening Dr. Shivapuri reminded the members of their past promise. The President and the Secretary of the Allahabad Branch both promised to do their best and to collect the money at an early date.

GENERAL PRACTICE DIGEST

TREATMENT OF PULMONARY EMPHYSEMA

In the treatment of the patient with emphysema its aetiology must be established. If it is secondary to bronchial asthma the treatment is primarily the treatment of bronchial asthma. These cases usually start with paroxysmal dyspnoea, frequently at night. The patient with primary emphysema early in his illness has dyspnoea only with exertion—his sleep is not interrupted. The patient with bronchial asthma may have rhinitis and nasal polyps, sinusitis and eosinophilia. The patient with emphysema and chronic bronchitis does not. In both cases x-ray examination shows hyperaeration. The bronchial asthma patient improves with adrenalin, while the primary emphysema patient shows little or slight improvement. The patient with asthma responds well to steroid therapy whereas patients with primary emphysema responds poorly with this drug.

All respiratory infections should be treated vigorously for an adequate period of time. The cause of infection should be determined and antibiotic treatment should be directed toward eradicating causal organisms.

If the patient has fever, procaine penicillin-G, 300,000 units should be injected every 12 hours. The patient's previous reaction to penicillin should be enquired into and a sensitivity test done before the injection. If the patient is sensitive to penicillin, erythromycin should be used.

If the patient has no fever, but is coughing out purulent sputum, erythromycin therapy should be started with a dosage of 250 to 500 mg. four times a day.

Once started, the antibiotic treatment should be continued for at least 10 to 14 days.

The patient should be kept active and should be instructed to continue his work. A less exacting job should be given to him. The patient should exert himself to the extent of his ability and shortness of breath is a warning sign, and rest is imperative. Dyspnoea of itself is not harmful.

The patient should be made comfortable. The tracheobronchial tree should be cleared of thick, tenacious and sticky secretions. Benefit is obtained from a saturated solution of potassium iodide, in dosage of 15 drops in half a glass of water, three or four times a day. It is the best type of cough medicine to give the patient with chronic emphysema. Cough mixtures containing codeine, morphine, or meperidine (demerol) hydrochloride should be avoided. Bronchodilators are of only limited value in the treatment of emphysema. Epinephrine (adrenalin) and ephedrine constrict mucosal blood vessels and improve air flow. If bronchodilators are given, they should be given both locally and systemically. Epinephrine (adrenalin), in a 1 :1000 solution, is given subcutaneously in doses of 0·3 c.c. Isoproterenol (aerosolised as a liquid or powder) is helpful in relieving spasm the patient may take 2 to 3 breaths of this, 3 or 4 times a day.

Types of Treatment

1. *Sedatives*—If the patient can breathe comfortably, he needs no sedative. Heavy sedation is hazardous be-

Facts and Figures

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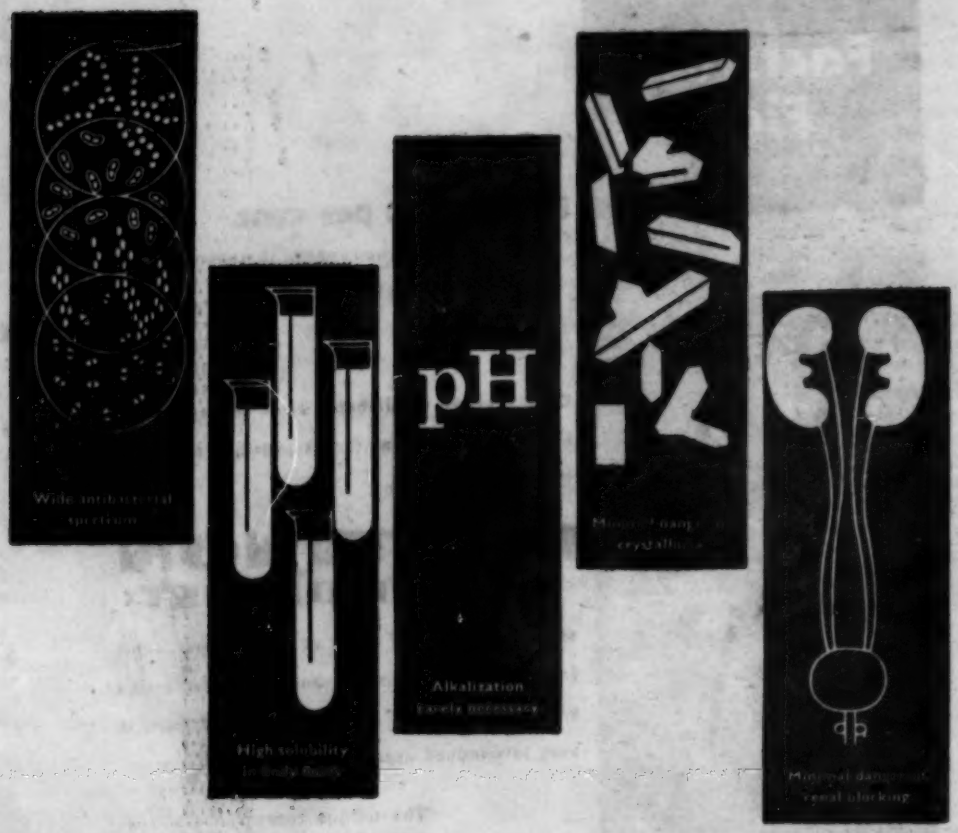

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cause these drugs depress the respiratory centre. Avoid the use of morphine and codeine. When a sedative is indicated, give phenobarbital in doses of 30 to 60 mg. or chloral hydrate in doses of 1 to 3 g.—as these drugs will produce mild sedation without depression of the respiratory centre.

2. *Oxygen therapy*—Hypoxaemia in a patient with emphysema, who is acutely ill with infection, is an indication for oxygen therapy. When the infection is over, he needs no extra oxygen. In the late stage of the disease, the patient feels more comfortable with oxygen. To avoid carbon dioxide narcosis, the patients are given oxygen therapy intermittently for 20 or 30 minutes each hour.

3. *Breathing exercises*—The patient is taught to breathe out slowly and with pursed lips.

4. *Intermittent positive-pressure breathing*—In this method, at the end of the patient's normal breath, additional gas is forced into the lungs which get distended. This method is not very helpful and there are certain disadvantages and dangers from its use.

5. *Steroid therapy*—These drugs are of little value in the treatment of primary emphysema. Patients with bronchial asthma respond well to steroid therapy.

6. *Pneumoperitoneum*—There is little objective evidence to support this therapy.

7. *Artificial ventilation with a respirator*—Hypoventilation is an indication for treatment with a respirator. This is most useful in patients with severe emphysema and an acute infection.

8. *Smoking*—Smoking is one of the causes of pulmonary emphysema. If possible, the patient should stop smoking. Some patients feel happy if they can smoke a few cigarettes a day. This should not be denied them.

9. *Surgery*—If a portion of the lung is cystic and over-distended, it compresses and prevents proper functioning of adjacent normal lung tissue. Surgical removal of parts of the lung is not recommended.

—From an article by George N. Bedell and Paul M. Seebohm—*J.A.M.A.*, **169**: 1702, 1959.

CURRENT MEDICAL LITERATURE

Iron Therapy in Chronically Fatigued Women

Beutler, E., Larsh, S. E. and Curney, C. W. (*Ann. Int. Med.*, **52**: 378, 1960) from the Argonne Cancer Research Hospital, operated by the University of Chicago for the United States Atomic Energy Commission, and the Department of Medicine, the University of Chicago, Chicago, Illinois, observe:

Symptomatic iron deficiency without anaemia has often been regarded as a clinical entity. Recent studies demonstrating that iron enzymes may be depleted in experimental animals with little or no lowering of the blood haemoglobin level lend a possible basis to the appearance of symptoms in nonanaemic, iron-deficient patients. However, no well-controlled studies have been carried out to determine whether nonanaemic patients may exhibit a genuine clinical response to iron therapy.

In the present study, iron and placebo were given to a group of women who complained of chronic fatigue but whose blood haemoglobin levels were above 12·0 g. per cent. Each woman received one period of iron therapy and one period of placebo therapy; the order of presentation of iron and placebo was varied at random. Comparative improvement in the two periods of therapy was correlated with independently determined measures of the body iron stores, viz., bone marrow stainable iron and plasma iron and iron-binding capacity. Haemoglobin determinations were carried out at intervals. Although the haemoglobin values of the patients were all within the normal range at the beginning of the study, an increase in the average haemoglobin level occurred in the iron-deficient group when they were given iron. Apparently, although the haemoglobin value of these patients was within the normal range, it was frequently below their individual norm. No significant change in the average haemoglobin level occurred in the group of patients with adequate iron stores, or in the iron-deficient group, during placebo administration. Of 18 iron-depleted patients, 13 manifested more symptomatic improvement with iron therapy than with placebo therapy, while five improved more with placebo therapy than with iron therapy. In contrast, of 11 women with only slightly reduced iron stores or normal iron stores, four improved more with iron, five manifested more improvement with placebo, and two did not improve at all. In view of these results, the possibility that nonanaemic women may benefit clinically from iron therapy deserves further study.

Chlorothiazide and Hydrochlorothiazide in Hypertension

Smirk, H., McQueen, R. G. and Morrison, R. B. I. (*Brit. M. J.*, **1**: 515, 1960) from the Department of Medicine, University of Otago, Dunedin, New Zealand write:

Chlorothiazide and hydrochlorothiazide are important additions to the list of hypotensive drugs, and in this respect seem equally effective in doses of 500 mg. for C. and 50 mg. for H.C. Both drugs enhance the effect of ganglion-blocking agents and diminish their requirement for satisfactory blood-pressure control with consequent diminution in parasympathetic side-effects. The enhancement is obvious with quaternary ammonium compounds as well as with compounds such as mecamylamine and pempidine.

Of 203 patients receiving these drugs, 15 per cent were managed most satisfactorily with C. or H.C. alone: 13 per cent were controlled by a combination with a rauwolfia alkaloid. Though these patients, assessed in terms of the basal blood-pressure as well as fundal grading, were somewhat less severely hypertensive than those requiring ganglion-blocking agents, nevertheless they included a considerable proportion with completing cerebral or myocardial ischaemia, making their management in other ways difficult.

H.C. certainly had less tendency to induce gastro-intestinal and possibly other side-effects. This gives it certain practical advantages over C. Care must be taken to avoid potassium depletion with both drugs.

Treatment of Tapeworm Infections in Man

JOPLING, W. H. AND WOODRUFF, A. W. (*Brit. M. J.*, **2**: 542, 1959) from the Hospital for Tropical Diseases, London give in the following lines the summary of their observations on the treatment of tapeworm infections in man:

Information on the results of treatment of tapeworm infections under standard conditions is scanty, and observations have therefore been made under such conditions in 240 cases.

No statistically significant difference in results was found between five different treatment regimes, including administration of male fern orally or by duodenal tube and of mepacrine by the same routes.

Factors which may give rise to poor results when these regimes are used include inadequate fasting, administration of male fern in capsules instead of in a draught, and, when doses of anthelmintics of small volume are administered through a duodenal tube, failure to take into account the amount required to fill the tube before any is delivered from its distal extremity.

Unfavourably false impressions of the efficacy of a treatment for tapeworms may be obtained unless patients are followed up for at least four months in cases in which the head of the worm is not recovered after treatment.

Failure of treatment due to vomiting was encountered more often among those treated with mepacrine than with male fern. As vomiting in patients with *T. solium* infections may give rise to cysticercosis, treatment with mepacrine in such cases is best avoided.

Griseofulvin in Infections of Scalp by Microsporum Canis

BEARE, M. AND MACKENZIE, D. (*Brit. M. J.*, **2**: 1137, 1959) from the Royal Belfast Hospital for Sick Children and Department of Microbiology, Institute of Pathology, Belfast, observe that griseofulvin is non-toxic to children in a dose of 0·25 g. three times daily for periods of up to 10 weeks.

Fungal invasion of hair is stopped abruptly soon after the drug is given, and new areas of infection do not appear. Debris, probably intrafollicular, remains infected and the organism can be recovered readily for long periods (up to 14 weeks) after treatment has started.

Wood's-light flourescence usually disappears in one to six weeks (average three weeks). With *M. canis* infections fluorescent tips are only exceptionally found.

In one rather unusual case in the series fluorescence was observed eight weeks after treatment had started; after the second week this fluorescence appeared at various distances from the surface of the scalp; positive cultures were obtained up to 12 weeks after the initiation of treatment, and microscopical examination often revealed a well-established infection in a non-fluorescent portion of hair.

Future studies should be directed towards a method for the removal of infected debris. Such methods might include washing, scrubbing, and/or shaving the affected areas, and the application of local fungicides. It is already apparent that, though griseofulvin is a most remarkable advance in antibiotic therapy, it is insufficient in itself to cure scalp ringworm (at least that due to *M. canis* within a reasonably short period).

Griseofulvin in Persistent Fungal Infections of the Skin

BARLOW, A. J. E., CHATTAWAY, F. W. HARGREAVES, G. K. AND TOUCHE, C. J. LA. (*Brit. M. J.*, **2**: 114, 1959) from the Department of Dermatology of Royal Infirmary, Huddersfield and Department of Dermatology of General Infirmary, Leeds observe:

Thirty-four patients with fungal infections of the skin have been treated with oral griseofulvin in a dosage of 1-2 g. daily.

Two children with candidiasis and one man with tinea versicolor showed no improvement.

Two patients infected with T. verrucosum derived no significant benefit.

Infection by T. mentagrophytes in one patient cleared after four weeks' treatment.

Two cases of T. rubrum infection of the smooth skin were treated for three weeks; one cleared completely and the other improved.

Twenty-six patients with long-standing T. rubrum infection with nail involvement were treated for periods of 3-20 weeks. The majority improved, but in only one instance was the infection eradicated.

Toxic reactions are recorded and possible reasons for the wide variations in clinical response discussed.

Follow-up Study of 500 Patients with Chronic Duodenal Ulcer

THOMSON, F. B., MCDOUGALL, E. P. AND MCINTYRE, D. I. (*Surg. Obst. & Gynec.*, **110**: 51, 1960) from the Department of Surgery, University of British Columbia Medical School, Vancouver, give in the following lines the summary of their observations on the follow-up study of five hundred cases of chronic duodenal ulcer:

Five hundred patients with chronic duodenal ulcer who were first admitted to Shaughnessy Veterans Hospital between 1947 and 1951 were studied.

In 63 per cent 1 or more complications developed during the clinical history.

Fifty-three per cent have already required definitive surgery; a further 43 per cent have significant continuing symptoms.

Intractable pain, the most frequent complication, was the indication for 57 per cent of all definitive surgery and was diagnosed only after unduly prolonged morbidity and economic loss because: (a) The characteristics of intractable pain in the patient's history were not conscientiously looked for. (b) The significance of rapid recurrence of pain in the patient's normal environment after temporary relief in the hospital was not appreciated quickly enough.

An episode of bleeding did not increase the likelihood that any particular duodenal ulcer would eventually require definitive surgical treatment.

Sixty-two per cent of postperforation patients required definitive surgery within an average time of 17 months for intractable pain or duodenal obstruction. The percentage requiring definitive surgical treatment was much higher in those with a preperforation history of over 1 year's duration.

Of 222 patients in whom vomiting occurred 68 per cent have already required definitive surgical treatment, 32 per cent have significant continuing symptoms, none has been cured. In patients whose vomiting was temporarily relieved by conservative means intractable pain or duodenal obstruction frequently developed for which definitive surgical treatment was required within a short period of time.

Organic duodenal obstruction, occurring to some degree in 17 per cent of patients and the indication for 30 per cent of all definitive surgery, was diagnosed very late because: (a) In 26 per cent barium meal studies failed to reveal retention. (b) Gastric residue was not measured until long after admission to the hospital. (c) It was not appreciated that weight loss, in the absence of vomiting, is often an early sign of slowly progressing duodenal obstruction and gastric retention.

When duodenal obstruction occurred it proved intractable to medical treatment in nearly two-thirds of patients upon diagnosis. In most of the remaining one-third, while responding temporarily, obstruction recurred and definitive surgery was needed in the first 2 years after diagnosis.

Effect of Childbearing on Rheumatic Heart Disease

MAYNARD, R. P. JR. AND GROVER, V. (*Ann. Int. Med.*, **52**: 163, 1960) from the Department of Medicine, the Brooklyn Hospital, Brooklyn, N.Y. and the Department of Medicine, State University of New York, Downstate Medical Centre, Brooklyn, N.Y. present a report of 455 cases of rheumatic heart disease in women of the childbearing age group, together with a report of a 25-year follow-up. These cases were analysed as to parity, nonparity, mortality, and the factors usually considered to be significant from a prognostic point of view, in order to answer the simple question: Does pregnancy affect the long-term prognosis in rheumatic heart disease?

It is pointed out that the selective effect of the very factor we are attempting to study creates a natural bias which precludes such data from providing an answer to the question we are studying. Therefore, this type of study cannot give us more than a clinical impression. The possibility that pregnancy in itself exerts a beneficial effect cannot be ruled out or investigated by these data. We can state that the more favourable experience of the parous woman probably results from a tendency of the nonparous not to become pregnant. However, there is certainly no evidence that pregnancy has a long-term detrimental effect in a large group.

Individually, pregnancy must be looked upon as a temporary hurdle, and each case must be considered individually. Undoubtedly pregnancy does in some individuals provoke or hasten invalidism and shorten life, as well as cause death, as Hamilton has pointed out. The incidence of cardiac failure and death is much higher during an individual year containing a pregnancy than in another comparable year in that same person's life. As he states, treatment markedly influences the over-all mortality, but only in "favourable" groups. In his experience, the mortality in the "unfavourable" groups is not greatly changed. Therefore, it is still the doctor's duty to weigh the relative risks of pregnancy in the presence of rheumatic heart disease, especially in the "unfavourable" cases early in pregnancy. A patient's death may not be statistically significant, but it can still be a great personal tragedy. In some cases, fortunately now very rare, therapeutic abortion may still be indicated.

Diuretic Treatment of Fluid Retention in Toxaemia of Pregnancy

FREIDBERT, V. (*German M. Monthly*, **4**: 418, 1959) from the Gynaecological & Obstetrial Clinic, University of Mainz, gives in a tabular form (*vide* Table below) the effects of 3 groups of diuretics used for treatment of fluid retention in toxaemia of pregnancy on the electrolyte changes in the serum and urine. The points emerging out of this observation must be taken into consideration before using these drugs.

	Mercurial diuretics	Hydro-chloro-thiazide	Carbonic-anhydrase inhibitors
Urinary sodium ...	++	++	+
Urinary potassium ...	φ	+	++
Urinary chloride ...	++	++	φ
Titratable acids ...	φ	+	−
Serum sodium ...	(−)	(−)	−
Serum potassium ...	φ	(−)	−
Serum chloride ...	−	−	φ
Serum carbon dioxide	+	+	−

The mercurial diuretics are not harmless when used in toxaemia of pregnancy; the potential danger of renal damage requires careful dosage and the marked electrolyte losses with sudden diuresis need careful attention.

Carbonic-anhydrase inhibitors are far less toxic than the mercurial diuretics, and the fact that they can be taken by mouth gives them an added advantage. However, they often are ineffective when used in toxaemia of pregnancy, and their effects on water and electrolyte balance and the not insignificant loss of potassium require continuous observation of the patient. Their rapidly decreasing effectiveness on continued use demands intermittent administration, which may lead to renewed oedema formation.

Hydrochlorothiazide is highly effective, causing marked diuresis without heavy loss of potassium and changes in acid-base equilibrium. It can therefore be used in outpatients and is effective in maintaining an oedema-free state until delivery.

CURRENT TOPIC

THE PRESENT STATUS OF THERAPY OF PLAGUE*

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Very little advancement seems to have been made on the treatment of plague over what was reported by Meyer *et al* (1952) and very ably summarised by Pollitzer (1954).

In regard to prophylaxis and vaccine therapy, it appears there is still enough scope for improvement. Plague was one of the most dreaded diseases until as late as 1940. The only treatment worth mentioning was the antiplague serum originally prepared by Yersin (1897), and perhaps the iodine solution as the only available chemotherapy. The use of sulphonamides 18 years ago greatly improved the prospect of curing bubonic plague. During the last decade the most outstanding success has been achieved in the treatment of all forms of the disease including pneumonic type by means of antibiotics, particularly streptomycin.

I. Serotherapy

The criterion of success of serotherapy, according to Sokhey *et al* (1952) was the results of treating cases of bacteraemia. While better results were obtained in treating milder forms of bubonic cases, the success was poor in septicaemic cases and very disappointing with primary pneumonic cases, except for the occasional success reported by Wu Lien Teh, 1926; De Moura *et al*, 1936; Joltrain, 1936 and a few others. In the earlier years of the last pandemic of plague in India, Choksey (1900) reported about 60 per cent of success in non-septicaemic cases. This was, however, the only available treatment at that time. According to Myer *et al* (1952) the pooled experience of the recent use of antiplague serum in the eastern hemisphere gives a fatality rate of 45·13 per cent in 3,840 treated cases against 83·5 per cent in 1,726 untreated cases. In the western hemisphere the fatality rate in 19,540 treated cases was 32·75 per cent against 74·07 per cent in 213 untreated cases. The latter data suffer from the defect of a small number of controls.

The most effective antiplague sera available recently are the ones produced against avirulent EV Madagascar strain and the Haffkine Institute plague serum. These have been used on a fairly large scale with better results. Girard (1941) and Le Gall (1943) reported about 60-65 per cent cure with the EV antiplague serum and Sokhey *et al* (1941-1948) 76·5 per cent overall cure in 157 cases treated with Haffkine antiplague serum only, but taking only 71 bacteraemic cases the rate of cure was only 49·3 per cent while only one death was registered among the remaining 86 cases. In another report of Sokhey, quoted by Meyer *et al* (1952) the case fatality rate in 163 serum treated patients was 20·6 per cent against 63·7 per cent in 135 untreated patients during the same outbreak (1948). The summary of the results is given in Table 1.

Table 1—Showing Summary of the Results of Treatment with Antiplague Serum (Meyer *et al*, 1952)

Area or place	Serum-treated cases		Untreated cases	
	Number	Fatality rate	Number	Fatality rate
1. Eastern Hemisphere (India, Indonesia, Japan, Middle East, Africa and Madagascar)	3,840	45·13	1,726	83·5
2. Western Hemisphere (North America, Argentina, Brazil and Peru)	19,540	32·75	213	74·07
3. Haffkine Institute (1941-1949)	320 (71 bacteraemic cases)	25·0 (50·7)	135	63·7

The initial daily adult dose of the present serum varied between 40 ml. advocated by Sokhey *et al* (1952) in bubonic cases and 100 ml. by Lobo and Silvette (1941) given partly intravenously and partly intramuscularly. Le Gall (1943) used 40-60 ml. of the serum prepared by EV strain. The serum was administered generally for two consecutive days for mild cases and up to five days in serious cases.

Production of Antiplague Serum—In 1931 Naidu and Mackie used virulent plague bacilli to prepare antiserum in buffaloes and reported encouraging results in bubonic cases at Hyderabad. But it was not defined how many bacteraemic cases could actually be cured. In 1936 Sokhey as also Girard (1936) utilised horses for serum production, as also Pirie and Grasset (1938). The mouse protection dose of the new Haffkine antiplague horse serum was 0·05 ml. as against 0·30 ml. of buffalo serum of Naidu and Mackie (1931) and 0·50 ml. of Lister and Pasteur Institute's sera (Sokhey, 1936; Sokhey and Dikshit, 1940) claimed 83 per cent cure of experimental plague infection in mice. In 1941 the workers at the Hooper Foundation, San Francisco, carried out a comparative trial of sera produced in horse, rabbit and guineapig on mice according to a standard technique and came to the conclusion that, to be effective, antiserum should be administered early (Meyer *et al*, 1952). The author (1943; 1953) noted better results with rabbit antiplague serum than with horse

* Summarised from a paper presented before the meeting of the WHO Expert Committee on *Plague*, Geneva, September 1958.

serum. This is supported by the observation of Meyer *et al* (1952) mentioned above. The most effective antiserum was the rabbit antiplague serum produced by injecting specific plague protein antigen isolated by the author. The author also wishes to mention that he succeeded in developing a quantitative precipition test and also a flocculation test by means of specific soluble plague proteins, for standardising the antiplague sera (Seal, 1954).

II. Sulphonamides

The most important factor which should be considered in the evaluation of results of treatment was mentioned by Sokhey and Wagle (1946), Meyer *et al* (1952), is the degree of septicaemia and clinical condition of the patient. Evaluation also depends upon the dosage of the drug its method of administration and supervision of the treatment. The required concentration of the drug in the blood is 5 to 10 mg. per 100 ml. (Wagle, 1948; Macchiavello, 1949).

The earliest compound tried was prontosil (p-aminophenyl sulphonamide) in 1938 by Carman (1938) and Vine (1928) and sulphanilamide by van Hoff (1938). Schutze (1939), Durand (1929) and Girard (1939) found sulphapyridine better than sulphanilamide. Soon sulphathiazole was discovered, followed successively by sulphadiazine, sulphamerazine and sulphamezathine; all were used for the treatment of plague in their turn. The combined experience of Sokhey and Wagle (1946) and Wagle (1948) in six field trials on all plague cases and also separately on septicaemic cases is summarised in Tables 2 and 3.

Table 2—Showing Results of Treatment of all Cases of Plague with Different Sulphia Drugs and Antiserum

Drugs or antiserum	No. of cases treated	No. survived	Percentage survived
Antiplague serum ...	157	120	76·5
Sulphapyridine ...	122	89	73·0
Sulphathiazole ...	345	266	77·1
Sulphathiazole+ antiserum ...	60	48	80·0
Sulphadiazine ...	168	152	91·5
Sulphamerazine ...	149	140	92·1
Iodine solution ...	149	69	46·3

It would appear from the data presented in Tables 2 and 3 that the sulpha drugs can be arranged in the following order of increasing efficiency: sulphapyridine, sulphathiazole, sulphamerazine, sulphadiazine, the last one having been found slightly more effective than sulphamerazine, particularly in septicaemic cases. The combined sulphathiazole and antiserum comes next best. In the hands of Sokhey and Wagle (1946) antiplague serum proved even better than sulphapyridine which, as it appears, cannot take care of the toxic or septicaemic cases as much as the antiserum or other sulpha drugs.

The combined results of treatment by all Indian workers with different sulpha drugs are summarised in Table 4.

Table 3—Showing Results of Treatment of Septicaemic Plague Cases by Different Drugs and Antiserum

Drugs or antiserum	Mild septicaemic cases (1-10 organisms per 0·25 ml. of blood)			Severe septicaemic cases (more than 10 organisms per 0·25 ml. of blood)			All septicaemic cases		
	Cases	Survivors	Per cent survived	Cases	Survivors	Per cent survived	Cases	Survivors	Per cent survived
Antiplague serum	29	22	75·8	42	13	38·0	71	35	49·3
Sulphapyridine	26	21	80·8	36	10	27·8	62	25	41·4
Sulphathiazole	27	23	85·2	104	53	50·1	131	76	58·0
Sulphathiazole+antiserum ...	4	4	100·0	21	13	61·9	25	17	68·0
Sulphadiazine	—	—	—	61	48	79·1	61	48	78·7
Sulphamerazine	—	—	—	22	15	68·2	22	15	68·2
Iodine solution control ...	19	5	26·3	56	2	3·6	75	7	9·4

Table 4—Showing the Combined Results of Treatment with Sulpha Drugs (Indian Data)

Drugs	Sokhey & Wagle 1941-1949			Simeons & Chhatre 1946 and 1947			Dutta Gupta 1948			Combined results		
	Cases	Survivors	Per cent survived	Cases	Survivors	Per cent survived	Cases	Survivors	Per cent survived	Cases	Survivors	Per cent survived
Sulphathiazole	345	266	77·1	142	116	81·7	—	—	—	487	382	78·4
Sulphadiazine	168	152	91·5	858	704	82·0	71	64	90·1	1097	920	83·8
Sulphamerazine	149	140	92·1	700	602	86·0	—	—	—	849	742	87·4
Sulphamezathine	—	—	—	—	—	—	37	33	89·2	37	33	89·2

The results given in Table 4 show that barring sulphamezathine which was used only in a few cases, sulphamerazine seems even superior to sulphadiazine, the Chi² test being 4·7896 for one degree of freedom. But Sokhey and Wagle (1946) found sulphadiazine superior in septicaemic cases and the Calcutta workers complained of kidney complications with sulphamerazine. Accordingly sulphadiazine has yet remained the drug of choice and, administered early, the results are very good.

The pooled results of the sulpha therapy given by Meyer *et al* (1952) also shows that sulphadiazine, which had been used in the largest number of cases, is the best, the survival rates with different drugs being as given in Table 4A.

TABLE 4A—SHOWING POOLED RESULTS OF SULPHONAMIDE THERAPY

Drugs	No. of cases treated	Survival rate %
Sulphanilamide	125	68·0
Sulphapyridine	725	45·4
Sulphathiazole	709	79·5
Sulphadiazine	1,061	91·4
Sulphamerazine	72	91·7

Doses—The doses advocated by Sokhey *et al* (1952) in the treatment of bubonic cases with different sulpha drugs are given in Table 4B.

TABLE 4B—SHOWING DOSAGE OF SULPHONAMIDES (SOKHEY *et al*, 1952)

Drug	Dosage	Remarks
Sulphapyridine and sulphathiazole	10-14 g. first day, 6 g. subsequent days up to 10 days depending upon severity.	The drug can be given intramuscularly or intravenously if needed.
Sulphadiazine	4 g. initial dose followed by 2 g. every 4 hours later. Thereafter 1 g. every 4 hours till the patient's temperature remained normal for 2 days.	Drug concentration 10-20 mg. per 100 ml. of blood.
Sulphamerazine	4 g. initial dose, followed by 2 g. 4 hours later. Thereafter 1 g. every 8 hours till the temperature is normal for 2 days.	Drug concentration 10-20 mg. per 100 ml. of blood.
Sulphamezathine (reported by Datta Gupta, 1948)	3 g. by intravenous injection then 2 g. 4 hourly for 4-7 days (per os.)	—
Higher initial doses are needed for septicaemic and pneumonic cases.		

The recommendation of the last WHO Expert Committee on Plague (1952) is given below.

In early cases of bubonic plague—10 g. on the first day followed by smaller doses to make up 50 g. in the first week. The first administration of 2 g. may be given intravenously or intramuscularly, preferably in glucose solution. The drug should be continued for 3 days after the temperature becomes normal in order to prevent relapses, and particularly in meningeal plague.

The advantage of chemotherapy in persons already immunised against plague has been shown by Patel and Rebello (1948), the percentage of mortality being reduced from 45·5 in the uninoculated to 21·6 in the inoculated group.

III. COMBINATION OF SERO- AND CHEMOTHERAPY

Perhaps a combination of sulphadiazine and antiplague serum would be an ideal combination, particularly for septicaemic and certain selected cases and streptomycin and antiplague serum for primary pneumonia cases. It is true that streptomycin by itself if often good enough for both types of cases. Including Schutze (1939), Girard (1939), Sokhey (1936) and perhaps Meyer (1951), the author thinks that combined administration of sulphonamides and plague serum is likely to give better results than either of them alone, particularly when the sulphonamides have no antitoxic action.

IV. ANTIBIOTIC TREATMENT

Just as in the absence of sufficient trial with sulphamerazine and sulphamezathine, sulphadiazine is considered to be the most tried and dependable sulpha drug for the treatment of plague including pneumonic cases, and among the antibiotics streptomycin has been found to be the most tried and effective drug. Penicillin has been found to have no effect at all in plague infection but it is used by some workers to prevent secondary lung complications.

The results of treatment with sulpha drugs have been well reviewed by Pollitzer (1954) in his book on plague. The rate of cure varied between 80 and 100 per cent. The total cases reported to have been treated between 1945 and 1953 was 786 with only 33 deaths, i.e., the cure rate was as high as 95·8 per cent.

Treatment of Primary Pneumonic Plague Cases—In regard to the treatment of primary pneumonic plague (summarised by Pollitzer, 1954), as many as thirteen workers reported cure in 24 of the 25 cases by streptomycin alone, whereas 9 other cases were treated without death by streptomycin combined with sulpha drugs, and sometimes in conjunction with penicillin and antiplague serum. The one case that died actually succumbed to a lung abscess not due to plague bacilli. In this connection Girard (1952) pointed out the necessity of using sulphonamides or penicillin as adjuvant treatment in such cases. The last Expert Committee therefore recommended that "in pneumonic plague, administration of sulphonamides or wide spectrum antibiotics might be necessary in order to prevent secondary infections or their sequelae."

In reviewing the recommendations of the last Expert Committee, the minimum dose for a plague case may be fixed in such a manner that the required concentration (5 to 10 mg. per 100 ml. of blood) of streptomycin may be maintained sufficiently long not only to bring the temperature down to normal as early as possible but also to maintain it at that position thereafter. It appears that the minimum dose in any case should not be less than 0·5 g. intramuscularly, to be repeated 4-hourly or at longer intervals if the case is mild, or at shorter intervals of 3 hours, according to the severity of the case. In cases of moderate severity, a dose of 2 g. per day may be the minimum and for frankly pneumonic cases a 2½-3 g. dose per day may be maintained until the case is considered safe enough from relapse or other complications.

In the treatment of bubonic plague sulphadiazine alone might be enough. In bubonic-septicaemic cases a few initial doses of streptomycin may be followed by sulphadiazine to complete the treatment.

Other Antibiotics—The success of treatment of human cases of plague with aureomycin was recorded by Ramchandran (1952), Meyer *et al* (1952). In the same year Girard (1952) and Mercier and MacCrumb (1952) reported successful results with chloramphenicol. The latter also treated five cases of pneumonic plague patients with terramycin.

According to Pollitzer (1954) antibiotics should be used only where specially indicated. The use of antiplague serum in addition to antibiotics, in special situations, may also be considered.

Other Treatments—These have been dealt with by Pollitzer (1954) under the items : (1) Rest in bed, (2) Diet and fluid intake, (3) Supporting treatment and (4) Treatment of buboes. While the clinicians will use their discretion in every individual case it may, however, be emphasised that particular care be taken that the patient is kept in complete bed-rest.

V. Chemoprophylaxis or Abortive Treatment

The author has obtained very good results in a heavily infected area where vaccination work against plague has been started, by giving exposed persons sulphadiazine in doses of 2 g. for the first 3-5 days in addition to the two doses of vaccine. During epidemics, many people escape the second dose either by chance or wilfully. This has been found to take off the incubatory cases which were not uncommon during the initial stage of the recent Calcutta epidemic and the vaccination drive. For the same reason, plague workers, even though they might have been protected by vaccination against plague infection, might fortify themselves with sulpha drugs at the start of an epidemic, at the initial stage of their work in the heavily infected areas and at the time of attending pneumonic cases.

Since the advent of the effective sulpha drugs, seroprophylaxis has been out of vogue. Even the contacts of pneumonic cases have been taken care of by sulphadiazine prophylaxis. Even so, one circumstance in which the author would still like to use seroprophylaxis is in the case of very close contacts of primary pneumonic cases, to whom potent antiplague serum may be given along with sulphadiazine or sulphamerazine.

VI. Vaccine Therapy

Plague vaccine is one of the earliest vaccines prepared by Haffkine (1897) for prophylactic use in human beings. Previous to him, Yersin *et al* (1895) had successfully immunised rabbits with related plague cultures. With the advancement of knowledge about the organism, its culture medium and growth factor, considerable improvement has been effected in the preparation of the plague vaccine. Even so, the results obtained regarding the value of the vaccine by different workers either in the laboratory or in the field have not been uniform. The method of preparation, the testing of potency and finally the statistical assessment of the field trials, all contribute some share in the make-up of this difference The two-dose vaccine has a special disadvantage for a mass vaccination campaign. Very often neither the people nor the field vaccinators are keen to follow up the vaccination with the second dose giving unsatisfactory results. The statistical evaluation is sometimes difficult in the absence of comparable controls.

There is sufficient evidence and field records available for the plague workers to come to the conclusion that vaccination against plague is of definite value in the prevention of plague.

Production of Effective Immunity after Vaccination—In a two-dose vaccine, as that of Haffkine plague vaccine, sufficient immunity to ward off a virulent infection may not be produced until seven days and a second dose is necessary to maintain the prolonged effect. It is therefore justifiable to think that persons who incubate the infection at the time of vaccination, or who become infected within five days of the vaccination, might develop plague. The fact that in one group there were 358 persons and in another smaller group, 74 persons (in Dharwar, India) among the recently vaccinated persons to develop plague within ten days after vaccination is itself evidence that protection was not conferred up to five days, taking the remaining five days as the incubation period.

From experience in both laboratory and field, the author wishes to suggest that during immunisation procedure man or animal remains at a disadvantage for 24-48 hours due to the lowering of normal antibody stock and in case of chance infection during these hours he is likely to come down earlier with symptoms than the uninoculated individual, as also observed by Simeons and Chhatre (1946, 1947). Although the preferable time for vaccination would be the inter-epidemic period, or at least three weeks ahead of the expected epidemic, in actual practice vaccination is resorted to when the epidemic is on.

In any case, since there is some chance of incubating the disease during a heavy epidemic, the author has suggested earlier than in such circumstances the first dose of vaccine should be followed by 2 g. doses of sulphadiazine or sulphamerazine for three to five days, which the vaccinator can verify when he comes there again seven days later for administering the second dose.

Recent Assessment of Antiplague Vaccine—Actual field trial data on a statistical basis for the assessment of antiplague vaccine are few. Among the recent Indian figures may be mentioned the data obtained at Kolhapur in Bombay by Patel and Rebello in 1948, and those of Calcutta and Gauhati (Seal, 1957). The results of administering a single dose of casein hydrolysate plague vaccine, grown at 32°C, are given in Table 5.

TABLE 5—SHOWING RESULTS OF VACCINATION IN THE INOCULATED AND UNINOCULATED

	Population at risk	Deaths	Mortality per 1000
Inoculated ...	282,816	509	1·8
Uninoculated ...	98,020	1,005	10·25

The mortality rate was 5·7 times more among the uninoculated than among the inoculated. This works out at only 17 deaths among the inoculated per 100 deaths among the uninoculated, giving a survival rate of 83·0 per cent. Even this is not good enough as by chemotherapy a higher survival rate has been achieved. In the 1948-1949 outbreak at Calcutta the fatality rate among 26 plague cases occurring among the inoculated was 11·5 per cent as against 20 per cent among the 310 uninoculated plague cases during treatment.

In Gauhati (Assam), however, only 4 cases occurred among the 50,000 uninoculated and no case among the remaining 50,000 inoculated persons. Absence of further cases may be due to other measures taken.

The varieties of vaccine which have been used from time to time are :

1. Killed plague vaccine
   (a) broth (Haffkine) vaccine
   (b) casein hydrolysate direct vaccine
   (c) agar grown vaccine
2. Live avirulent plague vaccine
3. Specific protein of plague organism—chemically prepared extracts
4. Other vaccines tried
   (a) pseudo-tuberculosis vaccine
   (b) lipo-vaccine
   (c) sugar vaccine
   (d) precipitated vaccine ... alcohol alum

1. *Killed plague vaccines*

Preparation of killed vaccine—The conditions precedent to the preparation of killed vaccine are the selection of a highly virulent plague organism and a suitable medium. In this connexion some workers like Schutze (1939) claimed no difference between virulent and certain avirulent strains. Although Sokhey and Habbu (1945) also obtained similar results (see protocol below), the latter workers did not advocate the use of avirulent strains due to variation in their antigenic value.

Vaccine	Mouse M.L.D.	Mouse protective dose
A	5	6·5 million
B	300 million	5·2 million

In regard to the question of toxicity and potency which were considered inter-related, recent work had shown that these two are not inter-related. The minimum doses of various killed vaccines which killed 50 per cent of white mice (26-278), as determined by Sokhey and Habbu (1945), are as given in Table 6.

TABLE 6—SHOWING RESULTS OF TOXICITY TEST OF DIFFERENT ANTIPLAGUE VACCINES

Vaccine	Toxic dose (ml.)	Mouse protective dose (ml.)
Haffkine broth vaccine (4 weeks' growth at 28°C)	0·2	0·0052
Agar vaccine (37°C) 1000 million per ml.	1·0	0·004
Heat (54°C)+phenol (0·5%) broth vaccine	0·2	0·006
Formalin (0·05%)+phenylmercuric nitrate 1 mg. per 100 ml. broth vaccine	0·4	0·006
Casein hydrolysate direct vaccine (killed by formalin 0·07%+1·5% phenylmercuric nitrate) ...	0·6-0·8	0·004

According to the above record, agar grown vaccine is the least toxic and the next best is the vaccine grown in casein hydrolysate broth, killed with 0·07 per cent formalin and preserved in 1·5 per cent phenylmercuric nitrate. This is the vaccine now used in India.

The protocol of doses of Haffkine Institute vaccine for different age and sex groups is given in Table 7.

TABLE 7—SHOWING PROTOCOL OF DOSES OF HAFFKINE INSTITUTE ANTIPLAGUE VACCINE

Age and Sex	Indian Standard		
	First dose (ml.)	Second dose 5-7 days later (ml.)	Annual revaccination dose (ml.)
Men	1·0	1·5	1·5
Women	0·75	1·0	1·0
Children :			
1—4 years ...	0·2	0·3	0·3
5—10 „ ...	0·3	0·5	0·5
11—15 „ ...	0·4	0·75	0·75

According to the experience of the author revaccination dose within one year after the primary vaccination in two doses need not be more than 0·5 ml. of any potent vaccine.

Siosteran
Intestinal antiseptic
without iodine
Agreeable coated tablets
Geigy
Made in India by:
Suhrid Geigy Private Limited,
Wadi Wadi, Baroda
Made in Switzerland by
J.R. Geigy S.A., Basle
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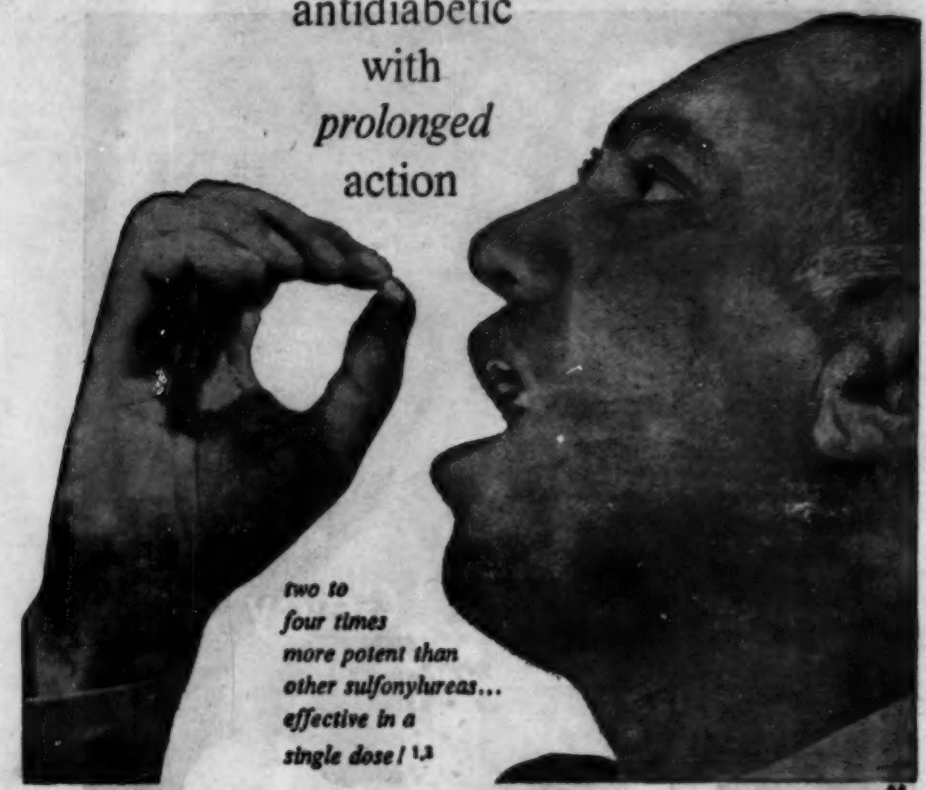

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Agar grown vaccine—As had already been shown, agar grown vaccine is less toxic than casein hydrolysate direct vaccine and equally potent, as tested by the mouse-protection technique. The most important point in regard to the agar vaccine is the quantum of organisms per ml. of the vaccine and the number of doses to be used. Different workers have advocated different concentrations of bacilli varying between 1000 to 3000 million per ml.

TABLE 8—SHOWING NUMBER OF BACILLI PER DOSE OF ANTIPLAGUE VACCINE

Authors	No. of bacilli/dose
Burgess	3000 million per ml. (1930)
Sokhey	1500 million per ml. (1939)
	1000 million per ml. (1958)
U. S. Army ...	2000 million per ml.
Barreto	1000 million per ml. (1938)
Lister Institute ...	1·5 mg. dried substance per ml.
Japanese	6 mg. sediment

Since the agar vaccine containing 1000 million organisms had the same mouse protection dose—0·004 ml.—as the casein hydrolysate agar (Sokhey and Habbu, 1945), the author wishes to suggest that if the organism is grown in a fully nutritive agar medium so as to allow the optimum development of the protective antigenic component, the agar-grown vaccine may be standardised at 2000 million organisms per ml. The first adult dose of such a vaccine should be 0·5 ml. followed by the second dose of 1 ml. one week later; or better still would be to adopt a standard as advocated by Meyer (1953).

Potency of killed vaccine and doses for field use—The potency of antiplague vaccine is tested in mice at the Haffkine Institute, but the adequate dose for human immunization has not been worked out on a thoroughly scientific basis. The calculated dose of organisms on the basis of mouse protection dose to immunise a man, according to Meyer, is 60 million, but man cannot tolerate even 15 million organisms. In other words, the dose that would protect a person from plague infection cannot be obtained from the present vaccine. Either a more potent vaccine should be prepared or only potent antigenic substances equivalent to 3 mg. of antigen (or 0·5-1 mg. of Seal's Antigen A) should be used.

2. *Live avirulent vaccine*

Pasteurella pestis is normally a delicate organism undergoing quick changes in an unsuitable environment. Virulent strains after several subcultures in agar lose virulence in no time. In fact, preservation of virulence of plague strains was a problem, but this was overcome by the author (Seal, 1943) by discovering a substratum for maintenance of the strain in freeze-dried conditions in sealed tubes containing inert gas. Virulent strains so preserved have been found to retain their virulence unabated even after twelve years.

Girard and Robic (1934) at Madagascar obtained a fairly stable avirulent strain called E.V. and Otten (1936) working in Java found a similar avirulent strain called Tjiwidej; the author came across another strain 53/Hav at Bombay in 1941. The author had the opportunity of working with all these strains. It is true that these strains have retained immunising properties almost equal to the virulent strains.

Both Girard and Otten obtained greater success with live avirulent plague vaccine in their respective areas, which led to the introduction of this kind of vaccine to many other countries like Argentina, Belgian Congo, Brazil, French West Africa, Tunisia and the Union of South Africa (quoted by Pollitzer, 1954); most of them found their own virulent protective strain. But Sokhey and his co-workers at Bombay did not agree to try such vaccines in India due to a certain amount of uncertainty prevailing in its nature, as corroborated by Devignat's (1949) recent observation of some temporary increase of virulence of E.V. strain. Very much greater control and supervision would be necessary to handle the vaccine preparation. Although the advantage was that it was effective in a single dose, the disadvantage of storing live vaccine and supplying it at short notice to distant parts of the affected areas was not a feasible thing under Indian conditions, and this and other considerations outweighed the advantage.

3. *Specific soluble protein of plague bacillus as antigen of choice for human immunisation*

The author (1943, 1951, 1953) produced experimental results to show that the immunising substance in the Haffkine plague vaccine or the plague bacillus is a specific soluble protein and that the potency of the plague vaccine depends entirely upon this specific soluble protein content of the organism or of the vaccine. Of the five fractions isolated, Antigen A, a polysaccharide-protein complex, specific in all respects to the virulent and avirulent protective plague strains, is obtained by precipitating the supernatant broth with 33 per cent satured Na_2SO_4 and is responsible for the protection. The human dose of Antigen A works out to be not more than 0·5 mg.

Besides Baker *et al* (1947), Amies (1951), and, more recently, Bhagavan *et al* (1953) isolated two or three protein fractions. The PD_{50} of fractions A and B of the latter workers were 8 and 8·3μg. respectively against a challenge dose of 100 MLD, which is also larger than the PD_{50} of Seal's antigen. The difference in the PD_{50} according to these workers might be due to the higher challenge dose used by them, i.e., 100 MLD as against 13 MLD by Seal.

The author, however, had the opportunity of verifying the relative values of Baker's antigen with his own in two ways.

While carrying out the transmission experiments in the domestic and semi-domestic rats, artificially immunised by Haffkine plague vaccine, Baker's Antigen I and Seal's Antigen A, a distinct difference was noted in the survival time between the vaccine immunised group and the protein-immunised group. On the basis of this observation he planned rat protection experiments in six groups of rats (3 *R. Rattus* and 3 *B.*

bengalensis) caught from the local field. For each type of antigen both *R. rattus* and *B bengalensis* (20 rats in each group) were used and immunised by two doses of antigen at weekly intervals. The challenge dose was 5000 virulent *P. pestis* 195/P. of Haffkine Institute given one week after the second dose. These rats were observed for a period of 30 days only. The results are summarised in Table 9.

TABLE 9—SHOWING RESULTS OF IMMUNISING DIFFERENT ANIMALS WITH VARIOUS PROTEIN FRACTIONS OF PASTEURELLA PESTS AS COMPARED WITH CH BROTH VACCINE

Antigen	Immunising doses	*R. rattus* (survival)	*B. bengalensis* (survival)
Seal's Antigen A	0·1 mg. divided into 2 doses	19/20	18/20
Baker *et al*'s Antigen*	0·1 mg. divided into 2 doses	16/20	14/20
Plague vaccine prepared in enriched casein hydrolysate broth (approx. 1000 million organisms per ml. killed with 0·1% formalin)	400 million divided into 2 doses	18/20	9/20

* This antigen was received through the courtesy of Dr. K. F. Meyer.

N.B.—The first figures in columns 3 and 4 indicate survivors up to 30 days after the challenge dose of 5000 organisms.

The results in Table 9 show that under the conditions of the experiment the antigen of the author depicted a higher protective value in the locally collected rats. One point which needs mention here is that Baker *et al's* antigen was used for this particular experiment one year after its receipt, while the Antigen A was almost fresh.

On the basis of the preliminary results mentioned above, it is proposed that this specific antigen be tried for human immunisation against the present Haffkine plague vaccine for which the possible advantages are: (1) exact dose required for protection can be accurately determined and administered; (2) volume of material to be injected will be small compared to the 2-3 ml. of vaccine now required; (3) less reaction than the present Haffkine plague vaccine; (4) reception of doses will also be easy, particularly if the reaction is negligible; (5) the immunity developed may be more prolonged than what is obtained by a single dose of fluid vaccine, (6) keeping qualities will be better; (7) it will permit a large stock to be prepared and maintained to meet any emergency.

If it is decided to use specific protein of plague bacillus the same may be easily obtained by precipitating the supernatant of enriched casein hydrolysate broth vaccine with 33 per cent saturation of sodium sulphate and then purifying the extract by a suitable method such as recommended by the authors Baker *et al* (1957), Amies (1951) and Bhagavan *et al* (1953). Even the precipitate obtained by 50 per cent saturated Na_2SO_4 may be used but the dose has to be standardised by mouse protection test of Sokhey or precipitin titre against a standard antiplague serum (Seal, 1954).

4. *Other vaccines*

The other types of vaccines that have been advocated as lipovaccine by the French worker Boye (1932, 1933) and alcohol-precipitated and alcohol-cum-alum precipitated vaccine of Wayson *et al* (1946) and sugar vaccine of Minervin *et al* (1935). The agents of killing the orgasisms have also been found to be important, formalin being found less disturbing than phenol and alcohol. However, it does not seem that these vaccines are in any way superior to the Haffkine plague vaccine.

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NOTES AND NEWS

WMA Aid to Earthquake Victims

The Secretary General of the World Medical Association has announced that Dr. Ernst Fromm, Treasurer of the Association, transmitted a check for $1,000 to the Secretary of the Colegio Médico de Chile to be used to provide medical assistance relief to the earthquake victims in Chile. Medical associations and doctors of the world are urged to provide medical supplies and funds for the relief of these victims. Assistance should be addressed to: Dr. Rolando Castanon, Colegio Médico de Chile, Miraflores No. 464, Santiago, Chile.

Medical Conference in Pakistan

The Pakistan Medical Association cordially invites representatives from the Medical Associations of the world to attend the VI Pakistan Medical Conference, Karachi, Pakistan, November 25-28, 1960. Additional information with respect to this conference may be obtained from: Dr. H. R. Khan, Secretary General, Pakistan Medical Association, Garden Road, Karachi.

Entries Invited for B.M.A. Prizes

The British Medical Association invites entries for the Sir Charles Hastings and Charles Oliver Hawthorne clinical prizes offered for the promotion of systematic observation, research and record in general practice. The prizes are respectively valued at £75 and £50. Any member of the B.M.A. engaged in general practice is eligible.

Entries are also invited for the Katherine Bishop Harman Prize for the encouragement of research into the disorders incident to pregnancy and childbirth. Any registered medical practitioner in the Commonwealth or Colonies or the Republic of Ireland or any member of of the B.M.A. wherever resident may compete. The value of the prize is £75.

Entries for all the three prizes must consist of original and unpublished material. Preliminary notice of entry is required. The closing date for the first two prizes is November 30, 1960, and that for the third is January 31, 1961.

Forms and further particulars may be had from: The Secretary, British Medical Association, B.M.A. House, Tavistock Square, London W.C. 1.

International Congress of Internal Medicine

The sixth International Congress of Internal Medicine, under the auspices of the High Swiss Federal Council, will be held at Basle from 24 to 27 August, 1960. The Swiss President Dr. Max Petitpierre is the Honorary President of the Congress. The President of the International Society of Internal Medicine is Sir Russell Brain. The President of the Congress Committee is Prof. Dr. A. Gigon of Basle.

A varied scientific programme of symposia, lectures and discussions will be held. All lectures as well as the scientific, the medico-historical, the pharmaceutical-technical exhibitions and the exhibition of books and periodicals will be held at the Swiss Industries Fair, Basle.

Correspondence should be addressed to: Sekretariat, 6 Internationaler Kongress für Innere Medizin, Steinentorstrasse 13, Basel, Switzerland.

International Tuberculosis Conference

The International Union Against Tuberculosis announces that the XVIth International Tuberculosis Conference will be held in Toronto, Canada, September 10th-14th, 1961, under the Presidency of Dr. G. J. Wherrett.

An interesting scientific programme has been arranged, as well as visits to hospitals and clinics. Tours in the City of Toronto and surroundings will provide opportunities to observe various aspects of Canadian life. There will be a full-day trip to Niagara Falls and pre- and post-convention tours in Canada and the United States. Special arrangements for travel, with reduced fares for chartered aircraft, will be made through national travel agencies.

Full details of the Conference can be obtained from the General Secretary, Dr. C. W. J. Jeanes, 265 Elgin Street, Ottawa, Canada, or Dr. Wm. Gellner, Executive Director, International Union Against Tuberculosis, 15 Pomereu Street, Paris 16, France.

Postgraduate Course in Nasal Surgery in Mexico City and Jerusalem

Thirty-six surgeons from the United States will be included in the faculty that will present an intensive, two-week postgraduate course in "Reconstructive Surgery of the Nasal Septum and External Pyramid," beginning July 4, at the Universidad Nacional Autonoma de Mexico, Facultad de Medicina, Mexico, D.F.

The other course on the same subject will be presented by the Department of Otorhinolaryngology of Mayer de Rothschild Hadassah University Hospital and the Hebrew University-Hadassah Medical School of Jerusalem in Jerusalem, July 31 to August 11.

The guest professor in Mexico City and guest director in Jerusalem will be Dr. Maurice H. Cottle, Professor of rhino-oto-laryngology at the Chicago Medical School, and founder of the American Rhinologic Society which will co-operate.

Antibiotic Plant in Chandigarh

On May 2nd, Shri Pratap Kairon, Chief Minister of Punjab, laid the foundation stone of the antibiotic plant being set up in Chandigarh by Dunmex in collaboration with Pfizer. It is designed for the basic manufacture in India of Terramycin and Tetracyn (5000 kilograms per year). The plant which is scheduled to go into production early next year will be able at full capacity to meet the requirements for the two antibiotics, in the domestic market as well as for export purposes. Apart from saving over a crore and half rupees' worth of foreign exchange, it will also mean that Indian technicians will get skilled, up-to-date training. The plant will have the benefit of all the research conducted by Pfizer throughout the world. It is expected that the products made in the Chandigarh plant, will undergo the same, strict quality tests that are applied to Prizer pharmaceuticals the world over.

Artificial Kidney for Bombay Hospital

An artificial kidney, a gift to India from Mr. Axel Johnson, a millionaire industrialist of Sweden, is shortly to be installed in the K.E.M. Hospital in Bombay. The apparatus helps a patient tide over crises arising from damaged kidneys which can be repaired. This will be the second centre in the country to instal an artificial kidney, the only other being the one at the Vellore Missionary Hospital.

Bombay Obstetric and Gynaecological Society Invites Theses for Prizes

The Bombay Obstetric and Gynaecological Society invites theses or essays for the award of the Dr. S. N. Bhansali Charitable Trust Prize and the Dr. Herculano De Sa Silver Jubilee Prize. The subjects for the first is "Any original work on human sterility", that for the second is, "Uterine action in pregnancy or labour." The values are respectively Rs. 500/- and Rs. 250/-. Fuller details may be had from the Honorary Secretaries, Bombay Obstetric and Gynaecological Society, Purandare Griha, Chowpatty Sea Face, Bombay.

REVIEWS

Modern Nursing : Theory & Practice—By Winifred Hector. 1960; William Heinemann Medical Books Ltd., London; 5½" x 8½"; pp. 515; price 30s.

It is a complete text book on nursing. In its pages will be found the experience of years in a great teaching hospital expressed in clear language by the Principal Tutor. The author has stressed the details she has found essential to an understanding of the functions and duties of a nurse.

There are 36 chapters and 145 illustrations. The first two chapters deal with the approach of a nurse to the patient as a human being. The rest covers all that a nurse should know—from the patient's toilet to the details of the various treatments she may have to undertake—medical, surgical, gynaecological and the specialities like the chest, ear, nose and throat, ophthalmology, urology, orthopaedics, etc. There is a section on operating theatre technique, the nursing of infectious diseases, tuberculosis, paediatric nursing, bandaging and first aid. There is also a chapter on the handling of psychiatric patients and one on the nursing of the aged.

This is a wise and satisfying book. If the nurse follows its teaching, she will be able to acquire the sense of fulfilment essential to the enjoyment of her calling.

STELLA JOHNSON

Antibiotic Therapy for Staphylococcal Diseases—Edited by Henry Welch and Maxwell Finland. Antibiotics Monograph No. 12, Medical Encyclopedia Inc., New York; 9" x 6"; pp. xii+208; price $4.50.

This volume is another addition to the Antibiotics Monograph Series, and has been brought out to help physicians and surgeons who are confronted with the problem of treating infections caused by staphylococci which have developed resistance to either penicillin or any one of the broad-spectrum antibiotics. The problem of emergence of resistant micro-organisms, specially that of staphylococci, has assumed gigantic dimensions in recent times It is now not merely confined to individuals or institutions but poses to be a public health problem.

In this book some of the antibiotics that have recently been discovered and developed have been elaborately reviewed. Special chapters, written by specialists, have been devoted to erythromycin, oleandomycin, novobiocin, vancomycin, restocetin and kanamycin. These are all antibiotics discovered during the post-penicillin era possessing antistaphylococcal activity. The details about each one of these have been given; their structure, field of activity, indications and contra-indications including their clinical appraisals and these go a long way in supplying information that should help the medical man to evaluate them. It is indeed an assurance to know that there are still some antibiotics available to control successfully, the obstinate staphylococci or some other equally adamant micro-organism. The role of kanamycin in the treatment of tuberculosis caused by *M. tuberculosis*

refractory to streptomycin and dihydrostreptomycin has been emphasised. The book could be considered as a valuable guide for the physician and the surgeon who are apt to come across during their daily routine practice cases of staphylococcal or other bacterial infections where the usual antibiotics fail to respond. It deserves wide circulation in this country particularly because staphylococcal resistance is coming to be one of the major therapeutic problems and it is desirable that safeguards and alternate arrangements be made in advance to control the situation when it arises.

There is a detailed bibliography at the end of each chapter. The binding and printing are excellent.

S. P. De

A Guide to the Identification of the Genera of Bacteria—By V. D. B. Skerman. 1959; The Williams & Wilkins Company, Baltimore 2, Maryland, U.S.A.; Bailliére Tindall & Cox Ltd., 7, 8, Henrietta Street, London W.C. 2; 9" x 6"; pp. x+217; price 44 sh. net.

This is a very useful supplement to the seventh edition of Bergey's Manual of Determinative Bacteriology. This compilation, thus, places in the hands of research workers, teachers and students, a volume in which general directives for the identification of bacteria have been supported by a complete list of techniques needed for the purpose. Thus, the detailing of the key as well as the methods in the presentation would be likely to encourage a more general application of the common procedures for the description of bacteria. The systematic bacteriologists should thus find the book very useful indeed.

D. C. Lahiri

Cates' Primary Anatomy—Edited by J. V. Basmijian, M.D. (Professor of Anatomy, Queen's University, Kingston, Ontario, Canada). Fourth edition, 1960; The Williams & Wilkins Company, Baltimore; 10" x 6½"; pp. 360, figs. 514, plates 14; price $6·50.

The usefulness and popularity of this book is indicated by the fact that it is now through its 4th edition. The book was originally written by Professor Cates to suit the requirements of non-medical students like nurses, physiotherapists, etc. The book as indicated by its name is an elementary treatise dealing in a systematic manner all the parts of the human body with particular emphasis on the locomotor and circulatory systems to suit the special requirements of the group mentioned. The book is written in clear, simple English and profusely illustrated with excellent diagrams in black and and white.

P. Bose

The Anatomy of Judgment—By M. L. Johnson Abercrombie, B.SC., PH.D. 1960; Hutchinson & Co. Ltd., London; 8½" x 5½"; pp. 156, figs. 12, plates 7; price 25s.

This book, new of its kind, is the outcome of ten years of experiments conducted in a class of senior students, in which usefulness of teaching methods by group discussions were put to critical analysis and attempts were made to evaluate the factors that lead to confident decisions. The book is divided into two parts, the first dealing with relations between inner and outer world, the various avenues through which information is received and their evaluations with reference to total situation and past experience of the individual. The second part is concerned with the principles of perceptions and their applications to make a valid judgment. It deals with students' way of thinking and how to help them to be more effective in drawing a correct inference of a situation. The book will make an interesting and useful study not only to the psychologists but for any teacher who is interested in developing a useful teaching method that may help his students to make well founded judgment.

P. Bose

OBITUARIES

Dr. R. P. Bhargava

Dr. R. P. Bhargava, M.B.B.S., D.P.H., passed away on February 1, 1960. After his medical education, he was appointed as the Executive Health Officer of the Indore Municipality and in course of time was promoted to the post of Assistant Director of Health, Madhya Bharat as well as Madhya Pradesh. He also officiated as Deputy Director of Health Services of Madhya Pradesh several times.

Dr. Bhargava was secretary of the Provincial Red Cross Society in Madhya Pradesh and vice-president of the Indore Branch, I.M.A. He took a responsible part in the 30th All-India Medical Conference, held at Indore.

He was an active member of the Indore Branch and took great interest in the affairs of the I.M.A. till his death.

Dr. R. M. Bhandari

Dr. R. M. Bhandari was born on July 14, 1902 at Udaipur. He graduated from the Grant Medical College, Bombay, in 1926. He joined the Holkar State Service as District Medical Officer in 1927, and rose to the rank of Inspector General of Hospitals in 1944. He became the Deputy Director of Health Services in Madhya Bharat in 1948 and was promoted to the post of Director of Health Services in 1955. After the formation of Madhya Pradesh, he was appointed as Inspector of Prisons and retired in that capacity in 1957.

Dr. Bhandari took great interest in the M. Y. Hospital and Medical College at Indore. He also took keen interest in the formation of Infectious Diseases Hospitals, as the member of the Municipal Corporation. He took keen interest in the welfare of the poor and was loved by all.

Dr. Bhandari was president of the Indore Branch, I.M.A., vice-president of the former Madhya Bharat

State Branch and vice-president of the Working Committee of the 36th All-India Medical Conference held in Indore.

Dr. Bhandari breathed his last on March 21, 1960.

DR. R. M. BHANDARI

DR. D. L. PATEL

Dr. D. L. Patel

Dr. Dahyabhai Lalbhai Patel was born in 1915 at Chijgaon. He had a brilliant career as a student. He graduated from the Grant Medical College, Bombay, in 1941. He was the first from his community to become a medical graduate. He started independent practice at Abrama and became very popular owing to his amiable and affectionate nature.

Dr. Patel breathed his last after a short illness on May 10, 1960.

Dr. Ida Scudder

Dr. Ida S. Scudder, founder of the Vellore Christian Medical College and Hospital, died at 7-30 A.M. on May 24, 1960. She was 90.

Dr. Scudder, daughter of a medical missionary in South India, saw too much famine, poverty and disease, and decided to study medicine. She took her M.D. at Cornell University, U.S.A. in 1899 and headed back to India fortified with a $10,000 gift from a Manhattan banker. With the money she started a tiny clinic for women at Vellore.

She established the Women's Medical School in Vellore in 1918 which later was reorganised and transformed into the Christian Medical College. The College was recognised and affiliated to the Madras University, on the occasion of the completion of fifty years' service in India by Dr. Scudder in 1950. Dr. Scudder won the Elizabeth Blackwell citation of the New York Infirmary, as one of the five outstanding women doctors of 1952.

Widely recognised as one of the best in India, the Vellore Hospital has topflight specialists from four continents. In addition, its four roadside bus clinics take care of villagers' health.

Dr. Scudder was very popular among the patients who were moved by her love, kindness and sefless service.

Dr. Sabita Ranjan Mukherjee

Dr. Sabita Ranjan Mukherjee, the seniormost physician of Suri (Birbhum), breathed his last after a brief illness on 28th February 1960. He belonged to the renowned 'Mukherjee' family of Suri.

Born on 16th October 1898, he received his early education at the Birbhum Zila School. He passed the B.Sc. examination from the Presidency College, Calcutta, and the M.B. examination from Calcutta Medical College in 1925. He then started his career as a private medical practitioner at Suri from where, after about 10 years of practice, he shifted to Chapra. In 1941 he received training in chest diseases and became attached to Chapra Sadar Hospital as a specialist in tuberculosis.

After 16 years he came back to Suri in 1946 and resumed private practice. He was attached to Suri Jail as T.B. specialist, was Hony. Visiting Chest Physician of Suri Sadar Hospital and connected with many other official and non-official institutions such as Police Hospital, Suri Vidyasagar College, Suri R. T. Girls' School and Beni Madhab Institution.

Dr. Mukherjee was a popular medical practitioner and was reputed for his kindness and straightforwardness. He was a member of the Indian Medical Association.

Dr. D. N. Banerjee

Dr. Deb Narayan Banerjee, a member of the Dooars Branch, I.M.A., passed away, at a comparatively early age of 44, on May 16, 1960 after a very brief attack of coronary thrombosis.

DR. D. N. BANERJEE

Dr. Banerjee qualified from the Jackson Medical School, Jalpaiguri, in 1938. He was actively associated with the Dooars Branch for the last ten years. He was also connected with many benevolent institutions and was loved by all.

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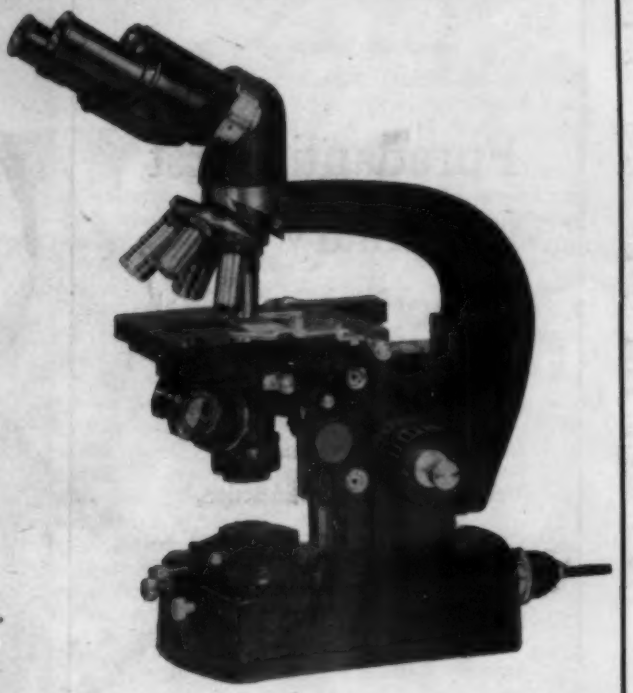

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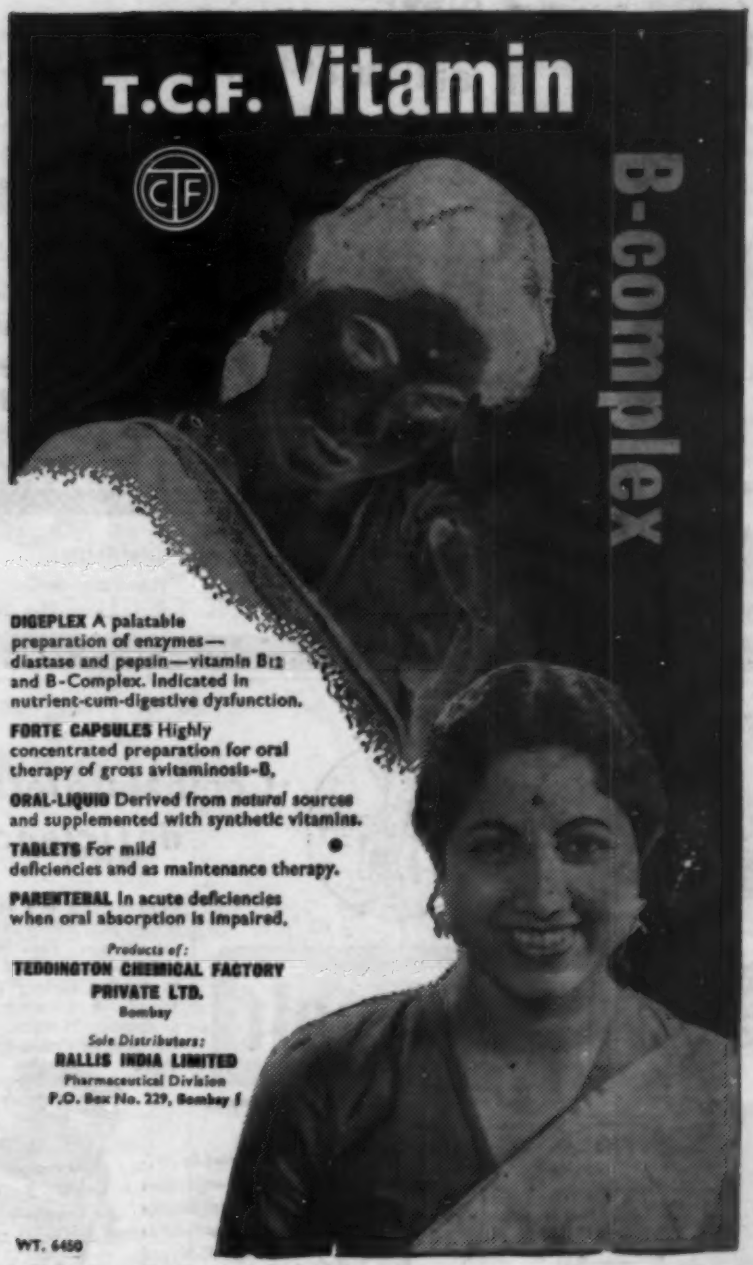

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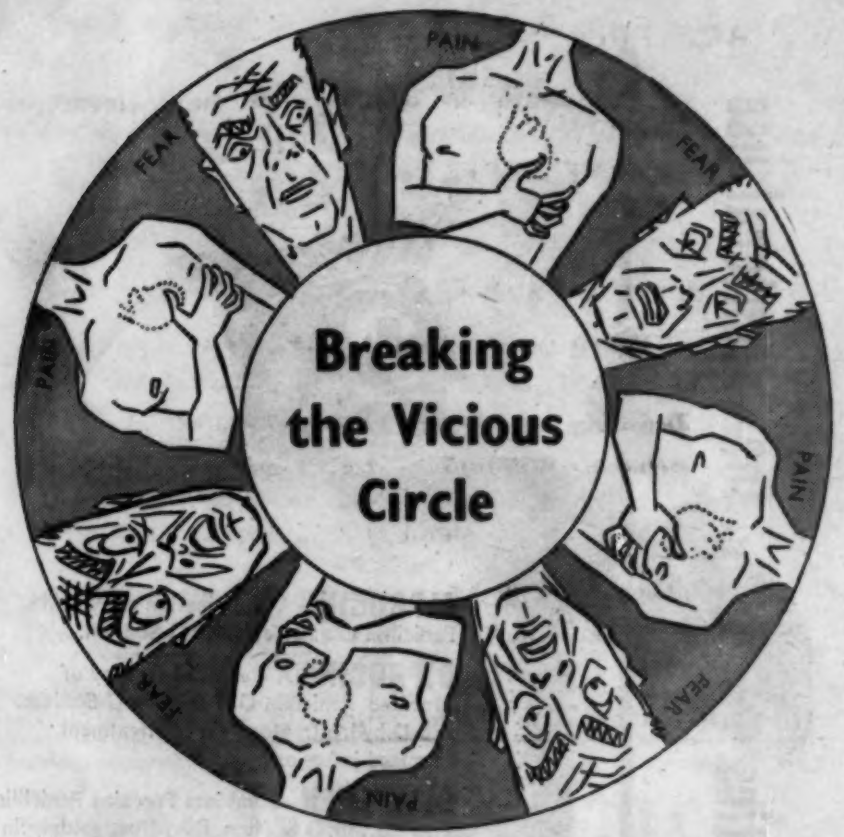

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1. Shapiro, S.: Angiology, 8: 504 (Dec.) 1957.

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Printed by Sri Tarani Kanta Basu at Sri Gouranga Press Private Ltd., 5, Chintamani Das Lane, Calcutta-9 and published by him on behalf of the Indian Medical Association from 23, Samavaya Mansions, Corporation Place, Calcutta-13.
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